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THE AMERICAN REVIEW OF TUBERCULOSIS

A Journal of Pulmonary Diseases

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MEDICAL SECTION OF NATIONAL TUBERCULOSIS ASSOCIATION

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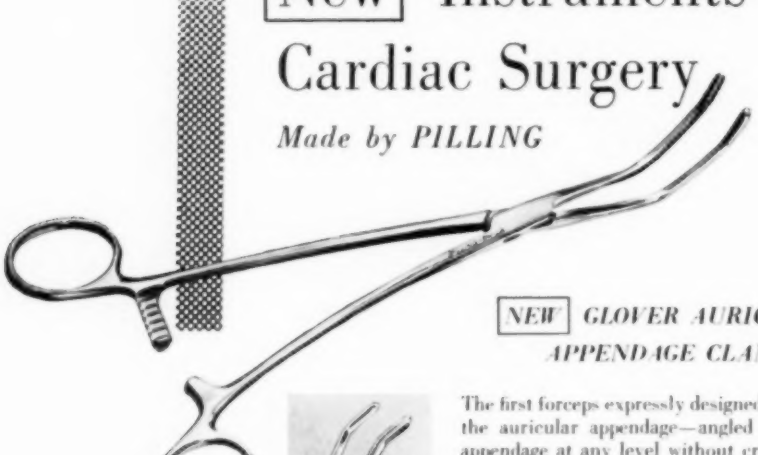

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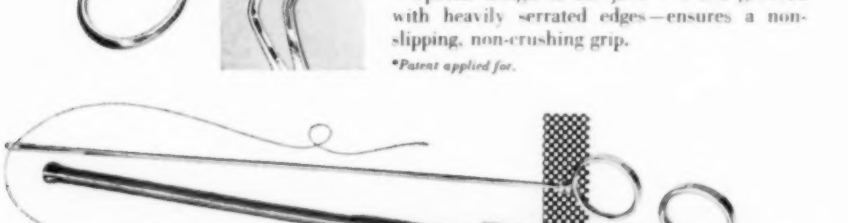

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1. Hobby, G. L., Lenert, T. F., Rivoire, Z. C., Donikian, M., and Pikula, D.: Am. Rev. Tubere. 67:808, 1953.

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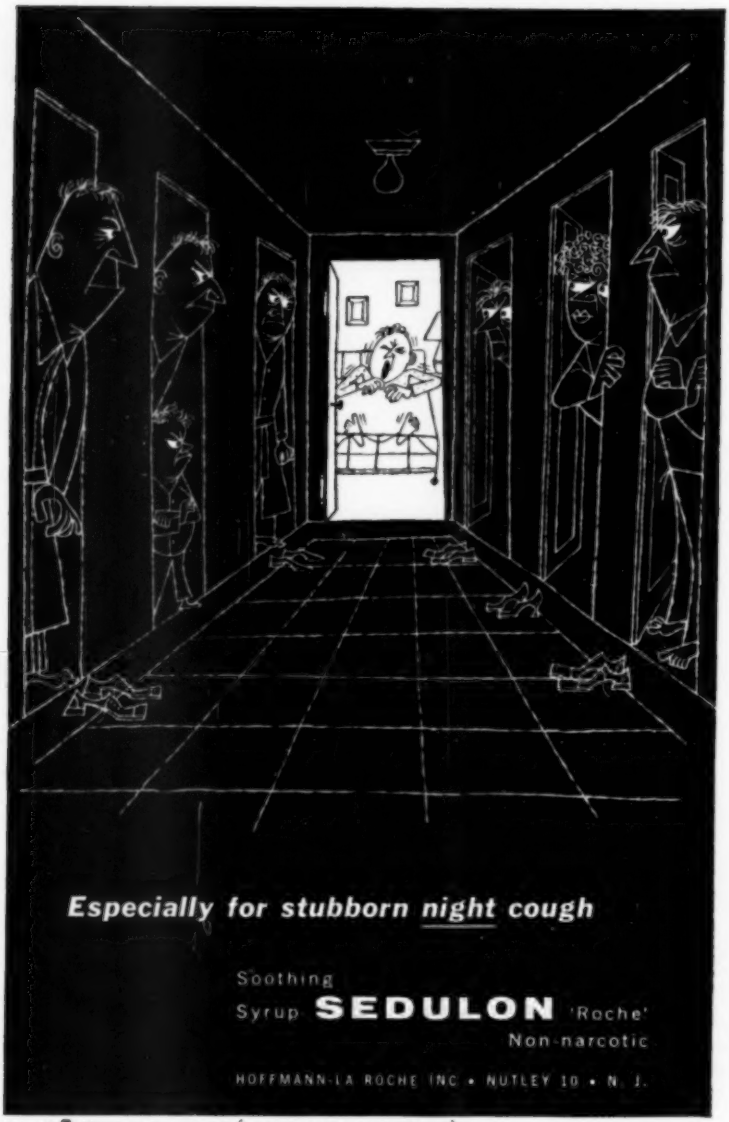

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THE AMERICAN REVIEW
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VOLUME 68 | *December, 1953* | NUMBER 6

TUBERCULOSIS IN HAWAII[1, 2]

HASTINGS H. WALKER

(Received for publication May 20, 1953)

INTRODUCTION

It may seem a paradox that tuberculosis, until very recently, has been the most serious health problem and major cause of death in Hawaii, the "Paradise of the Pacific." The statistical data alone by no means reveal the severity of the problem in the past or the favorable changes in recent years. Perhaps, the observations and impressions gained from many years devoted to tuberculosis in the Islands will serve to round out the picture more completely and permit the telling of the very dramatic story of this disease in Hawaii.

THE SETTING

These beautiful Islands and their colorful history have been adequately recounted by writers and poets through the years. The rhapsodies will be left to these worthies and the writer shall only say that to him the Islands are more lovely than could ever be described in words. The tourists are generally unaware of the patches of gloomy darkness which at one time marred this beautiful setting. These patches must be scrutinized for a true understanding of the appalling health conditions of the past.

Brief attention must be given to the environmental setting. Hawaii comprises a cluster of small islands, remote in the Pacific, roughly 2,100 miles from California. The land area of the seven inhabited islands is 6,407 square miles (1). Although they lie at the northern edge of the tropics, the climate is generally subtropical. At low land levels, where the greatest proportion of the people dwell, there is nearly perpetual summer with but slight range in temperature and humidity, relatively low rainfall, and sunshine for the greater part of the daylight hours. In Honolulu, the capital city, the annual average temperature is 75°, the average humidity 72 per cent, and the average rainfall 25 inches (2). Such a gentle, equable climate, with abundant sunshine and adequate rainfall, permits a high degree of outdoor living and obviously has a most significant influence on health. As some wit has said, "Hawaii has the climate that Southern California advertises" (3).

[1] From the Leahi Hospital, Honolulu, Hawaii.

[2] Presented in part at the *Opening General Session* of the annual meeting of the National Tuberculosis Association, Los Angeles, California, on May 18, 1953.

The composition and growth of the population have had an important bearing on the economic and social structure of the Islands. Additionally, public health and disease incidence have been profoundly influenced by the "melting pot" of races, their complex process of acculturation, their admixture, and their unusual age and sex distribution. At the time of discovery by Captain Cook in 1778, rough estimates of the population of Hawaiians varied from 300,000 to 400,000. In 1836, a census made by schoolteachers under direction of the missionaries showed a dwindling to approximately 110,000 (4). Kingdom censuses in subsequent years revealed a continued precipitous decline to a low of 56,897 in 1872 (1). At this point there commenced a great upswing in growth as successive waves of Chinese, Japanese, Koreans, Portuguese, Puerto Ricans, Filipinos, and others came to the Islands as plantation laborers. By 1900, Hawaii was a United

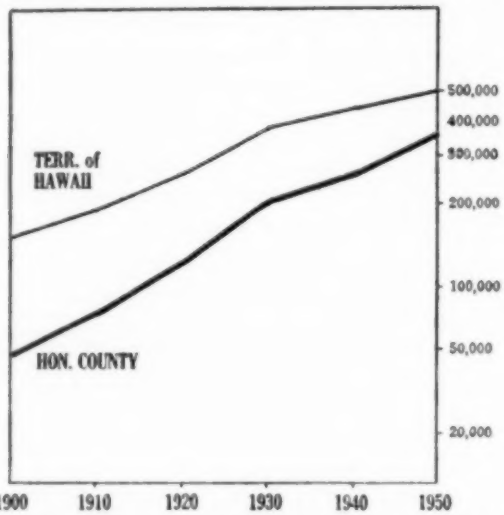

FIG. 1. Population of the Territory of Hawaii and the County of Honolulu.

States territory and the population had reached 154,001. Figure 1 shows the subsequent growth of the Territory to 499,794 in 1950, with Honolulu County reaching 353,020. The rapidity of growth since 1900 is attributable chiefly to continued importation of plantation workers, immigrations from the mainland United States, and excess of births over deaths.

Since 1910, accurate records of births and deaths have been kept by the Board of Health, and from 1917 the Territory has been included in the U. S. Registration Area. The birth rate, though declining since a peak of 41.6 per 1,000 (5) in 1925, is still high (30.1 in 1950) (6). The crude death rate has declined steadily through the years from very high levels to the exceedingly low rate of 6.2 per 1,000 (6) in 1950 (United States 9.6) (7).

In table 1, giving the population by race and sex, several features are revealed

which have very important bearing on the incidence and control of tuberculosis. The large numbers of persons of races with high susceptibility and the extreme difference in sex distribution are especially noteworthy. The age distribution is of decided significance, for Hawaii, generally speaking, is a youthful community. Although recent years have seen a slow aging of the population, a greater proportion is still of younger age than is the case in the mainland. The median age for Hawaii in 1950 was 24.9 (8), the median age for males being somewhat higher than that for females (26.2 and 23.6, respectively).

Economic and social conditions: The sugar industry has been the keynote of Hawaii's economic wealth during the past one hundred years, thus accounting for the diversity of races as well as the hitherto predominantly rural distribution

TABLE 1

POPULATION OF THE TERRITORY OF HAWAII BY RACIAL EXTRACTION AND SEX DISTRIBUTION

U. S. Census Figures

YEAR	HAWAIIAN	CAUCASIAN	CHINESE	FILIPINO	JAPANESE	OTHERS	TOTAL
Per Cent Distribution Both Sexes							
1900	19.3	23.8	16.7	—	39.7	0.4	100.0
1910	20.1	23.0	11.3	1.2	41.5	2.9	100.0
1920	16.3	21.4	9.2	8.2	42.7	2.2	100.0
1930	13.8	21.8	7.4	17.1	37.9	2.0	100.0
1940	15.2	24.5	6.8	12.4	37.3	3.8	100.0
1950	17.2	23.0	6.5	12.2	36.9	4.2	100.0
Males per 100 Females							
1900	110.5	126.8	642.4	—	349.2	185.5	223.3
1910	104.4	128.6	378.9	944.7	220.1	437.3	178.9
1920	101.6	125.9	221.6	403.1	134.3	229.7	144.3
1930	99.4	153.8	156.0	501.3	116.1	159.1	152.8
1940	99.4	164.0	127.6	346.3	110.3	124.3	137.6
1950	98.8	132.4	111.2	248.7	102.1	131.6	121.2

of population. Next in importance is the pineapple industry. The tourist business within the past five years has come to occupy third place. Well over half of the food supply is derived from outside sources, chiefly the mainland United States (9).

Honolulu today is a very modern American city of more than moderate size and is the center of the governmental, financial, and industrial life of the Islands. Its people today, despite the many racial backgrounds, for the most part live very much as do the people of the average mainland city. The average earnings of Hawaii's workers compare favorably with the earnings of those in similar occupations on the mainland (8). The cost of consumer goods and building are high, as are taxes (10).

Vital statistics and health: Although health and sanitation in the Islands are

generally of high standard now, the situation was decidedly otherwise in former years. Many factors accounted for the magnitude and complexity of the health problems of the past. Because of its location at the crossroads of the Pacific, Hawaii was a highly vulnerable target for a variety of communicable diseases. With the arrival of large numbers of foreign plantation laborers, many diseases were introduced, together with many foreign attitudes toward public health and sanitation. The failure to provide adequate sanitation and public health measures to deal with the overcrowding in shack-like dwellings and horrible tenements concurrent with the rapid swelling of population, especially in the last quarter of the nineteenth century, was an additional factor of great moment.

The change in the health picture during the past fifty years is indicated by the following: a lowering of the infant mortality rate from 279.6 per 1,000 live births in 1900 (9) to 23.6 in 1951 (6) (one of the lowest rates ever recorded for any state or territory); a drop in the crude mortality rate from 25.1 per 1,000 in 1900 (9) to 6.2 in 1950 (6); no locally contracted smallpox in thirty-eight years; no deaths from diphtheria in six years; no deaths from typhoid fever in more than four years; and no deaths from whooping cough in more than three years.

EARLY HISTORY OF HAWAII

The early history of Hawaii is of exceptional interest from the standpoint of the upheaval in the culture and health of a primitive people which resulted from the arrival of foreign races. Of equally great interest is the vivid history of the development of public health measures which were undertaken to overcome the dreadful health and sanitary conditions which followed on the heels of this invasion.

The Hawaiians are of Polynesian origin and are believed to have migrated to the Islands from the Society Islands (Tahiti) by canoe in successive waves during several hundred years (11). Recent evidence establishes the fact that the natives were living in Hawaii at about 1000 A.D. (12). Contact with other peoples was probably nonexistent until the arrival of Captain Cook in 1778. His accounts, together with those given by later explorers and the missionaries, indicate that the primitive natives lived an almost idyllic life with an ideal climate, abundant sunshine, and plentiful food. The authorities agree that the native Hawaiians were physically of a superior type, having great strength, beauty, and grace. Until the advent of the white man, it appears that there was little overcrowding in their small settlements near the sea. Their well-ventilated grass dwellings provided adequate shelter, and sanitation was probably far superior to that prevailing in many towns and cities of Europe and America at the time. As one writer (13) puts it:

> Two centuries ago white standards of cleanliness were low at best: the vermin and stenches of the great towns of Europe would have sickened the average Polynesian. . . . Nor did such standards as there were appeal to seamen who, in that day, were mostly too shy of water even to learn to swim as a safety measure. Fo'c'sle Jack, pursuing a Maori girl reeking with fish oil, probably smelled even worse than she did.

Life was generally out of doors, the sea occupying an important part in their lives. Food was plentiful, healthful, and nutritious. The diet was high in carbohydrates, with "poi" as the staff of life. Fish, shellfish, and meat (chiefly hog and dog) provided adequate amounts of protein and fats.

Robert Louis Stevenson did poetic justice to the Hawaiian people when he said:

> . . . a lovely week among God's best—at least God's sweetest works—Polynesians. . . . I know no race that carries years more handsomely, or whose people, in the midst of life, retain more charm. I recall faces, both of men and women, with a certain leonine stamp, trusty, sagacious, brave, beautiful in plainness: faces that take the heart captive (14, 15).

With the coming of the whites—explorers, whalers, and missionaries—evil and, to a decidedly lesser extent, good influences came into play to precipitate a calamity, with tragic effects upon the Hawaiian people. All too true is the sayings, "The virtues and arts of civilization are almost as disastrous to the uncivilized as its vices" (16). Despite the missionaries' earnest endeavors to "Christianize" the Hawaiians, their influence must have been slight in stemming the tide of evil brought by the increasing numbers of ships, whose crews polluted the place with vice, venereal disease, and liquor. The Reverend Mr. Cheever (17) called Lahaina, the prominent Hawaiian whaling haven, "one of the breathing holes of Hell."

It is readily understandable why these people became crushed in spirit and why their numbers decreased at such a dreadful rate. Newly introduced disease usually attained epidemic proportions, taking an appalling toll of lives. Additionally, a high infant mortality, rapid dilution of the race by admixture, and profound changes in living habits all played their part in the near destruction of the race. An early writer (4) in 1838 says, "The great majority of children born in the Islands die before they are two years old."

HISTORY OF HEALTH AND DISEASE

Prior to Captain Cook's arrival, the Hawaiians obviously were not free from disease. However, the pertinent point is that their diseases were comparatively innocuous, compared with the disease killers introduced by the early explorers, sandalwood traders, whalers, and missionaries.

One of the earliest known medical writings on the disease incidence in Hawaiians is that of Alonzo Chapin (18) in 1838 in which he said, "The variety of their diseases is neither numerous nor complex. Their remoteness from other lands is so great that but few contagious diseases are imported among them." As will be pointed out later, however, those "few contagious diseases" were prone to assume epidemic proportions.

In order to appreciate the disastrous effects produced by the introduction of communicable diseases to the natives, one must realize that various epidemics were raging throughout the world and, moreover, knowledge of public health and sanitation was practically nonexistent.

The earliest recorded epidemic disease was in 1804, considered by many to have been Asiatic cholera (19). It was evidently widespread and very deadly for, according to Wood (20), it destroyed about half of the native population. From then on throughout the nineteenth century, the Islands experienced a series of epidemics, usually of widespread occurrence and attended by shockingly high mortality (21). Except in the case of smallpox, which in 1853 caused death in 2,109 of the 5,686 cases reported in Honolulu, the effects of pestilential diseases (cholera in 1895 and bubonic plague in 1899 and 1900) were localized and took but small toll. By all odds, the most widespread and fatal of the epidemics were the repeated attacks of measles, whooping cough, scarlet fever, influenza, and "diarrhea"—the typical story of "childhood disease" in non-immune people. Each of these successive epidemics killed by hundreds or by thousands, accounting in large measure for the rapid depopulation which occurred during the first hundred years after the arrival of the whites. A characteristic example was a serious epidemic of "fever" (probably scarlet fever) which struck the Islands in 1870. In the melancholic words of Dr. Stover, a practicing physician on Maui, "The mortality on the Island is shocking. I never knew until now that people could die so easily or with so much indifference" (21).

The first physicians came to the Islands after the arrival of the missionaries in 1820, prior to which time the only real medical attendance had been that given by passing ships' surgeons. It is interesting to note that the first little hospital, for seamen, was set up at Waikiki in 1837. Hitherto, sailors, when ill, had been quartered in private homes or in the grog shops of Honolulu. The numerous visitations of severe epidemics became of serious concern to the Hawaiian Kingdom and led to the establishment of a Board of Health in 1850—indeed, a very early date when one considers that the English Public Health Act was passed in 1848 and that California's Board of Health was established in 1871.

It is believed that leprosy, "mai pake" (Chinese sickness to the native Hawaiians), was first introduced in 1840. By 1863 it had reached alarming proportions, and the health authorities began to take steps for its control. The story of the Molokai leper settlement and its role in the control of this disease is well known. By approximately 1873, leprosy had become epidemic and, as might be surmised, the Hawaiians were most severely afflicted.

Late in 1899, bubonic plague paid a visit to Honolulu and in a matter of hours flamed into an epidemic which struck terror to the citizens. It was short-lived, however, as the result of prompt and decisive action by the authorities, in addition to a great fire which burned the plague spot, Chinatown, to the ground. It was a costly and harrowing experience but the loss was to be more than reconciled in subsequent years as the result of the community's rude awakening to the need for a sanitary clean-up. Fear provided the necessary stimulus to action. The people were determined upon the elimination of insanitary conditions in order that Hawaii would be proof forever against the introduction and spread of serious contagious diseases so that the land, once again, would be a place of unmarred beauty where life would be comfortable, enjoyable, and healthful. The people commenced their enormous task, and their achievements are readily apparent in the completely changed picture of today. In all probability, there

was little realization that the attack upon the foul environmental conditions was destined to play an immensely important role in the future control of tuberculosis.

TUBERCULOSIS—EARLY HISTORY

The early history of tuberculosis in Hawaii is lost in obscurity. The first observers, including the physicians of the voyages of discovery who described health conditions in the native Hawaiians, notably failed to mention consumption. Dr. G. P. Judd (22), in 1837, indicated that it was of rare occurrence although "scrofula was very common." He noted the frequency of other lung disease, particularly "asthma, pleurisy, and pneumonia". Dr. Alonzo Chapin (18), in 1838, also pointed out that catarrh and asthma were "very common but mild" and that "consumption seems to have been entirely absent."

There is food for thought in those early writings. Actually though, no one knows whether tuberculosis existed prior to the arrival of Captain Cook, but evidence strongly points to its introduction at that time or shortly thereafter. In all probability, the disease had already been implanted, perhaps in one or more areas on one or more of the Islands, by the time of the arrival of the missionaries in 1820. The behavior of the disease in primitive peoples, as indicated by Cummins (23) and others, would lead to the belief that it very likely remained localized in small foci in the widely separated villages for a considerable period, taking its toll for a time in small numbers. It was inevitable, though, that the time would come when the smoldering foci would flare into a widespread epidemic of extreme fatality. Since the women would be hit hardest during their early years of childbearing, it is readily understandable why tuberculosis played so great a part in decimating the race through ensuing years.

Apparently, little attention was paid to tuberculosis in early years, the chief health concern being the repeated epidemics of acute contagious diseases. However, Cheever (17) did say, in 1851, that "many die of induced phthisis and consumption of the lungs is frequently the termination of long ailments."

By the beginning of the last quarter of the nineteenth century, it was all too evident that the disease was of extreme prevalence. By 1886, Captain Brown, the health officer, was reporting that consumption was increasing, with one in every eight deaths due to this cause (21). Hoffman (24) stated that, in 1892, the prevailing diseases among Hawaiians were pulmonary tuberculosis and various forms of kidney and liver troubles.

By the turn of the century, the health officials fully recognized that they were faced with an overwhelming problem of tuberculosis which was of very great complexity because of several unique factors. The health officials and leading citizens of the community were convinced that tuberculosis could be controlled, and they set to work on the problem with as much determination and courage as they had manifested throughout the great epidemics of the past.

THE TUBERCULOSIS SITUATION FROM 1900 TO THE PRESENT

The phenomenal change in tuberculosis mortality in the Territory and Honolulu since those gloomy days of 1900 is clearly shown in figure 2. Particularly

remarkable has been the precipitous drop since 1947. There were only 72 deaths from tuberculosis in the entire Territory in 1952, 43 being in Honolulu. It should be stated that the 1951 and 1952 provisional rates are probably on the high side. The National Tuberculosis Association gives a rate of 13.7 (25) for Hawaii in 1951, whereas the Territorial Board of Health gives 14.7 for that year and 15.5 for 1952.[3] The use of different population estimates probably accounts for the discrepancy.

As has been true in the United States as well as in the other countries which have shown progressive decline in tuberculosis mortality during the twentieth century, marked improvement in living conditions was the dominant factor in causing the decline in Hawaii for at least the first thirty years or more. There is very good reason to believe, however, that the cumulative effects of Hawaii's control program were being manifested before the onset of World War II. Furthermore, the evidence strongly suggests that specific measures have played the leading role in the dramatic change since 1948.

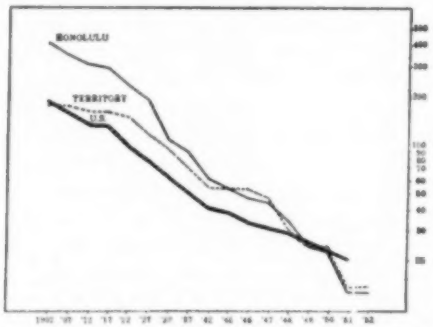

FIG. 2. Tuberculosis mortality rates per 100,000 for the United States, Territory of Hawaii, and Honolulu by five-year averages through 1944 and annually thereafter.

Mortality rates obviously did not reveal the true state of affairs during the first decade or more. There are several reasons for believing that the deaths from tuberculosis in the early years were far in excess of those reported. For instance: there was a very high incidence of unattended deaths, especially among Hawaiians and Orientals dwelling in rural areas; there was very poor reporting; there was an excessively high number of deaths reported as being due to pneumonia and acute bronchitis, which very probably could be attributed to tuberculosis in many instances; the practice, until 1947, of listing all deaths among lepers as due to "leprosy," when, in fact, a predominant cause of death was tuberculosis; and lastly, the lowering of both the mortality and morbidity rates in consequence of the considerable number of Japanese, Filipinos, and others who returned to their native lands once tuberculosis was diagnosed.

In table 2 is shown in a striking manner how Hawaii has changed its rank

[3] The Territorial Board of Health reports provisional tuberculosis death rate of 11.1 per 100,000 for the fiscal year ending June 30, 1953.

TABLE 2

TERRITORY OF HAWAII TUBERCULOSIS MORTALITY RATES AS COMPARED WITH STATES
1943–1951

Death Rate per 100,000 Population

1943			1951		
Puerto Rico	231.1		Puerto Rico	117.0	
Arizona	125.9		Arizona	64.5	
New Mexico	72.8		District of Columbia	36.7	
District of Columbia	67.2	10	Nevada	33.8	
Kentucky	64.0		Kentucky	33.7	
Tennessee	63.6		New Mexico	32.2	
Maryland	57.6		Maryland	30.3	
HAWAII	57.2		Tennessee	29.6	
Colorado	51.3	9	Alabama	25.4	
Louisiana	50.8		Virginia	24.8	
Arkansas	49.9		Texas	24.8	
New York	49.9		Louisiana	24.5	
Nevada	48.8		New York	23.3	
Texas	47.0	8	Mississippi	22.4	
Virginia	45.4		Pennsylvania	22.1	
New Jersey	45.2		Illinois	21.3	
California	45.0		Missouri	21.3	
Missouri	43.9		Colorado	20.2	U. S. MEAN
Alabama	43.7	7	New Jersey	19.8	20.1
W. Virginia	43.6		Georgia	19.6	
Massachusetts	42.3		California	19.4	
U. S. MEAN 41.9 Illinois	42.1		W. Virginia	19.3	
Oklahoma	41.8		Delaware	18.8	
Montana	41.1	6	Massachusetts	18.5	
Ohio	40.4		Vermont	18.5	
Georgia	39.8		Florida	18.4	
N. Carolina	39.7		Oklahoma	18.1	
Pennsylvania	39.6		Ohio	18.1	
Rhode Island	37.7	5	Michigan	17.8	
Delaware	37.0		Arkansas	17.5	
Indiana	35.8		S. Carolina	16.7	
Vermont	35.7		Rhode Island	16.5	
Washington	35.3		Maine	15.9	
Florida	35.2	4	N. Carolina	15.2	
Mississippi	35.2		S. Dakota	14.9	
Connecticut	33.7		HAWAII	14.7	
Michigan	33.2		Indiana	14.4	
S. Carolina	33.1		Connecticut	14.1	
Maine	31.9	3	Montana	14.1	
Minnesota	29.2		Oregon	13.5	
N. Hampshire	27.8		Washington	12.8	
S. Dakota	26.7		N. Hampshire	11.1	
Wisconsin	24.9		Wyoming	10.5	
N. Dakota	23.0	2	Kansas	9.9	
Oregon	21.9		Wisconsin	9.8	
Kansas	20.4		N. Dakota	9.5	
Wyoming	17.3		Nebraska	8.7	
Idaho	16.9		Minnesota	8.5	
Iowa	16.4	1	Utah	7.8	
Nebraska	16.2		Idaho	7.7	
Utah	10.3		Iowa	6.3	

From N.T.A. Bulletin 1944

From N.T.A. Bulletin 1952

among states as the mortality rate has dropped since 1943. That the reduction has occurred in all races, including the vulnerable Hawaiians, is demonstrated in figure 3. For better graphic presentation, the four middle racial groups are depicted in a band, the rates for each race being shown in the order in which the races are named in the legend, with the Filipinos highest and the Japanese lowest.

The mortality by age has shifted dramatically, especially in the last decade, as may be seen in figure 4. The contrast between infants and young adults as compared with older age groups is noteworthy. The morbidity shift parallels this trend, a point of utmost significance from the standpoint of future emphasis in case finding and control. In substance, tuberculosis seems to be on its way to

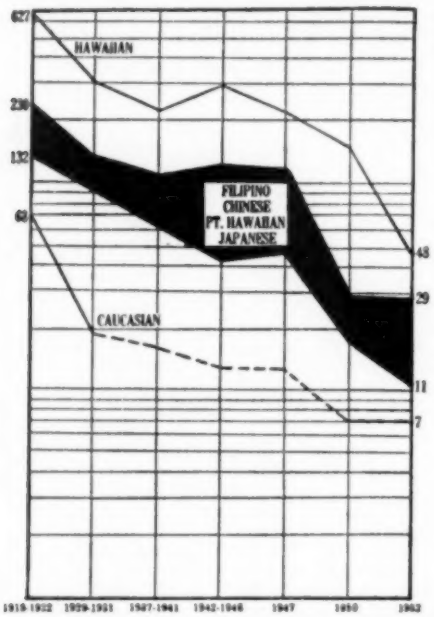

FIG. 3. Tuberculosis death rates by race; territorial mortality per 100,000.

becoming a disease of elderly or middle-aged people. The assumption, perhaps, is warranted that the lowered mortality and morbidity in the young reflect a material reduction in the opportunities for acquiring massive infection, whereas the older age curve represents the end stages of infection acquired in past decades. Further evidence of this trend is indicated in table 3, which gives proportionate mortality by age since 1918. Whereas the percentage of deaths due to tuberculosis was 11.6 in 1918 for all age groups, it was only 4 in 1950.

Particularly noteworthy, however, is the change which has taken place in the younger age groups. In 1918, 26.2 per cent of all deaths in children aged five to fourteen years was due to tuberculosis, but in 1950 there were *no deaths* from the

disease in this age group! Furthermore, in the fifteen to twenty-four age group, the percentage of deaths due to tuberculosis dropped from 30.5 in 1918 to 5.4 in 1950. It must be pointed out that a trend in this direction had already occurred by 1940, so that chemotherapy and surgery cannot be given the entire credit. It should be emphasized, however, that, although tuberculosis in the very young is becoming a rare occurrence in Hawaii, it is by no means benign when it does occur. This is borne out by the fact that, despite a marked reduction in admissions of the very young to Leahi Hospital in recent years, the few who are admitted, as

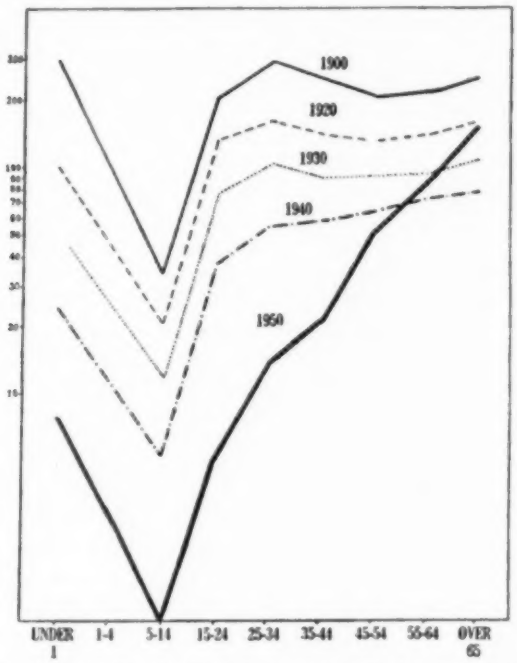

FIG. 4. Tuberculosis death rates by age groups; territorial mortality per 100,000.

a rule, have serious disease, with one or two cases of meningitis admitted annually.

Morbidity trends: It is apparent from figure 5 that Hawaii, like many states, has shown relatively little change in the registered case load despite the mortality decline. Additionally, there has been no appreciable drop in the known active cases. Intensive case finding by mass roentgenographic surveys, together with a change in the system of reporting in 1947 to conform with Public Health Service standards, accounts in the main for the great increase in registered cases commencing with 1946.

Factual data on morbidity have been decidedly less reliable than the mortality

figures, especially during the early period. There is sufficient evidence, however, to show that the disease was extremely prevalent at the turn of the century and

TABLE 3

PROPORTIONATE MORTALITY FROM TUBERCULOSIS BY AGE SHOWING CHANGES SINCE 1918
TERRITORY OF HAWAII

	1918			1930			1940			1950		
	All Deaths	Tuberculosis Deaths	Per Cent Tuberculosis	All Deaths	Tuberculosis Deaths	Per Cent Tuberculosis	All Deaths	Tuberculosis Deaths	Per Cent Tuberculosis	All Deaths	Tuberculosis Deaths	Per Cent Tuberculosis
All ages	4,010	466	11.6	3,865	392	10.1	3,025	266	8.8	2,883	114	4.0
Under 1	1,538	8	0.5	890	13	1.5	459	1	0.2	335		
1–4	359	19	5.3	344	15	4.4	111	2	1.8	82	2	2.4
5–14	191	50	26.2	167	28	16.8	99	4	4.0	45		
15–24	298	91	30.5	273	77	28.2	181	39	21.5	92	5	5.4
25–44	750	92	12.3	674	144	21.4	517	117	22.6	311	28	9.0
45–64	684	105	15.4	899	96	10.7	846	72	8.5	873	47	5.4
65 and over	370	24	6.5	618	19	3.1	812	31	3.8	1,145	41	3.6

Compiled from the Annual Reports of the Territorial Board of Health.

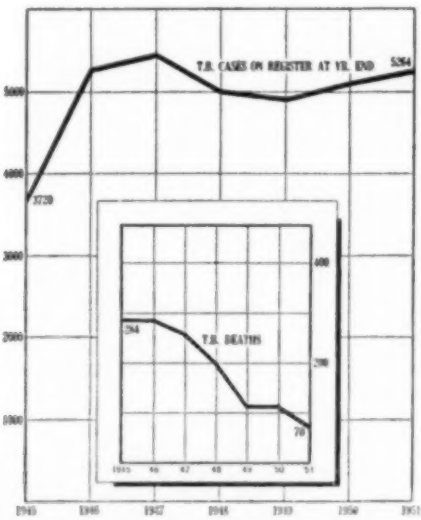

FIG. 5. The number of tuberculosis cases registered at the end of each year, 1945–1951, and the number of tuberculosis deaths in the Territory of Hawaii for similar years.

that it exhibited certain characteristics worthy of mention. It should be borne in mind that Hawaii is a relatively youthful community, with an excessive proportion of males over females. These two features obviously had a bearing upon the

age and sex incidence of the disease. It is not surprising, therefore, to find that the peak age of reported cases for many years was in the age group twenty to twenty-nine for men as compared with the age group ten to nineteen for women (6).

There has been a very definite progression upward into the older age groups, as is demonstrated by the shift in age of patients admitted to Leahi Hospital. In 1932, for example, 64 per cent of the 383 patients admitted were less than 35 years of age; whereas, by 1952, there had been an almost complete reversal, 56.6 per cent of 395 persons admitted were more than thirty-five. Even more striking differences have been noted with respect to the very young: only 13 patients admitted in 1952 (total, 395) were under the age of fourteen; whereas, twenty years ago, 52 of 383 persons admitted were in this age category.

Another favorable change is the marked decrease in morbidity and mortality from nonpulmonary forms of tuberculosis in more recent years. In 1924, for example, of 1,000 new cases reported to the Tuberculosis Bureau, 14 per cent were nonpulmonary, listed as follows: miliary, 7; meningitis, 14; abdominal, 32; Pott's disease, 26; tuberculous joints, 32; other organs, 31 (6). In 1931, 9 per cent of the deaths and 16 per cent of reported cases were nonpulmonary and, in that one year, 125 (10.7 per cent of total new cases reported) were listed as "lymphatic" (6). The improvement in this phase of the problem is indicated by the register figures of 1952, which show that only 4.8 per cent of newly reported cases were nonpulmonary. As will be noted later, tuberculous lymphadenitis and bone and joint involvement were very prevalent in children in the first quarter century. Hawaiians were especially prone to exhibit nonpulmonary forms of disease.

As might well be expected, there was a great racial difference with respect to morbidity, severity, and types of disease. The Hawaiians and Samoans, by all odds, had the highest incidence and the most severe forms of disease, with the Filipinos, another highly susceptible race, as a close second. The Caucasians have always had a low incidence, and the Orientals spread out between the two extremes.

Interestingly enough, the part-Hawaiians have shown much lower morbidity and mortality rates than the full-blooded Hawaiians for many years. Halford's (26) tuberculin survey of 382 Hawaiian and part-Hawaiian boys and girls (age range thirteen to eighteen) at Kamehameha School in Honolulu showed that 75.9 per cent of the Hawaiians reacted positively, whereas the figure for Asiatic-Hawaiians was 70.6 per cent and that for Caucasian-Hawaiians 56 per cent. Some of the studies on primitive tuberculosis, such as those by McGibony and Dahlstrom (27) in their work with Montana Indians, have offered suggestive evidence that genetic admixtures with a susceptible people tend to lower the mortality rate and perhaps the incidence.

Standards of living, nutrition, and environmental factors no doubt played the most important role in the marked differences in Hawaii's racial groups. Other factors, however, must be considered. The Hawaiians, and likewise the small number of Samoans in the Islands, in addition to their generally poor living conditions and hygiene, showed great reluctance to seek medical care and accept

hospitalization. They were largely uninterested in the health education program. Those who could be persuaded to enter a hospital were usually in a far advanced, if not terminal, state and were all too prone to leave before treatment was concluded. This situation has changed notably in recent years, particularly with the younger people. Despite the extensive case-finding program, a few Hawaiians who have never had roentgenograms are still admitted with far advanced disease. All too frequently, such patients are from families with a notorious tuberculosis history. But in contrast to former years, many more Hawaiians are now entering the hospital with early disease. Furthermore, they are now much more likely to remain in the hospital and, in general, respond to chemotherapy about as well as the other races.

Most of the other races presented their own characteristic problems which were very likely to have a deleterious effect on the course of their disease. As has been pointed out by Burrows (28), the adaptation of Hawaiians and Orientals to an American way of living was invariably slowest with respect to food, language, and religion, as the result of early conditioning. Since primitive "healing" may be considered a part of religion, it is not surprising that health education, according to Western concepts, made but little, if any, impression upon the older people.

Particular mention must be made of the Japanese, to whom tuberculosis was a great social stigma. As a consequence, the first generation Japanese in Hawaii were exceedingly reluctant to accept a diagnosis of tuberculosis. They were prone to refuse hospitalization until too late and, in many instances, would elect to return to their native country. Since they constituted the largest racial group in the Islands, they have been the largest group in our sanatoriums. It may be said, in passing, that the Japanese almost invariably have been ideal patients in every way and that their response to treatment has been good. In contrast with the first generation, the younger Japanese people have readily absorbed health teachings and, almost without exception, when diagnosed, accept hospitalization without the least hesitancy.

The contrast in tuberculosis mortality rates of the Japanese in Hawaii as compared with the rates in Japan is of interest. In Hawaii, the rate for the five-year period, 1918 through 1922, was 132 per 100,000 as compared with 12 in 1952 (6). In Japan, on the contrary, the rate for 1918 through 1922 was 233 and, in 1951, the last available figure was 111 (29). Similar differences exist in other races such as the Filipinos, Chinese, and Koreans, all having much lower rates in Hawaii than those reported in their respective countries of origin. In all probability, higher living standards and better nutrition are the most important factors to account for these differences.

As an indication of the poor nutritional state of some of the races during the early period, it should be pointed out that beriberi was common in the first twenty years or more of this century, particularly in Filipinos and Orientals. During the five-year period, 1902 through 1906, there were 200 deaths from beriberi, the highest mortality rate being 3.7 per 1,000 in 1902 (24). From 1912 to 1915, beriberi was the fourth cause of death in Filipinos, 10.5 per cent of all

causes. In the writer's early days at Leahi Hospital twenty-five to thirty years ago, beriberi and pellagra were by no means uncommon but neither disease has been observed for several years. The older Orientals presented difficult problems in hospital treatment because of their rigid adherence to long-accustomed native foods. This was particularly true of milk, which was apt to be completely foreign to their diets.

PRESENT TUBERCULOSIS CONTROL PROGRAM AND ITS DEVELOPMENT

It is unfortunate that Robert Koch's epidemiologic studies in tuberculosis and his brilliant grasp of the fundamental measures for its control are so little known today. In his Nobel lecture at Stockholm in 1905 (30), he set forth in a masterly fashion the basic principles which he predicted would virtually reduce the disease to insignificance, *if vigorously carried out.* It is generally forgotten that Robert Koch established the pattern which so many states and nations are presently following, at least to some degree. His measures were:

> (*1*) The "notification of discovered cases," which carried with it an assumption that physicians would be competent in establishing a diagnosis; (*2*) "isolation," with respect to which he said that "if it were possible to assemble these open cases all together in hospitals and render them relatively harmless thereby, then tuberculosis would very quickly die out." He cited in this connection the example of leprosy control in Norway; (*3*) "clinics" for those unable to obtain hospitalization; (*4*) "health education."

Significant is his remark that the battle against tuberculosis is fundamentally a question of money and that the financial outlay must be great.

It is interesting to note that, at the turn of the century, when Hawaii's health authorities became aware of the magnitude of their tuberculosis problem, they established basic principles for the guidance of their control program which differed very little from Robert Koch's pattern. Except for modifications in applications and methods, together with the added feature "follow-up and rehabilitation," these original principles have been followed throughout the years with ever increasing intensity.

Isolation and treatment commenced on a very small scale with the opening of Leahi Hospital in Honolulu in 1902; a surprisingly good educational program was put into effect in 1909; and a Tuberculosis Bureau was established by the Board of Health in 1910 for registration of cases.

Obviously, these first steps had little, if any, immediate effects.

Bovine tuberculosis: Before showing the growth of these control measures and their accumulative effects in later years, it is necessary to mention at this point the attack upon bovine tuberculosis which began in 1910 and undoubtedly left its mark at an early date. At the turn of the century, dairy sanitation was unusually bad, and the veterinarians were drawing attention to a high incidence of tuberculosis in beef cattle. The health authorities worked steadily to improve this situation and succeeded in their efforts, for today the dairy standards are of the best.

Victor A. Norgaard (31), territorial veterinarian, castigated the medical profession and health authorities in 1914 for failing to recognize the importance of bovine tuberculosis in their "anti-tuberculosis program." He proceeded to show the work of the Board of Agriculture in tuberculin testing of cattle. In 1910, the first year of this work, it was found that 32 per cent of the dairy cattle supplying milk to Honolulu were tuberculous! At the end of the first three years, however, the percentage of reactors had been reduced to 1.5 per cent. A continuous, vigorous tuberculin testing program has been carried out throughout the Territory ever since, and for some years now the reactor rate has been consistently below the accepted standard of 0.5 per cent. Pasteurization of all milk sold has been in effect for a number of years, with 97.7 per cent pasteurization in the Territory as a whole. Consequently, the chance of acquiring bovine infection from milk purchased in Hawaii has been virtually nonexistent for several years. The "family cow," however, still presents an unknown hazard.

Although no real study of the problem has ever been conducted, sketchy data and clinical impressions have led the writer to the belief that bovine tuberculosis once played a very significant role, especially in the infection of children. Previous mention has been made of the incidence of nonpulmonary forms of tuberculosis in the early decades. Scrofula and bone and joint tuberculosis were fairly common in children and young adults treated at Leahi Hospital in the nineteen twenties and thirties. During the past ten years, these conditions have been rare except when a part of generalized tuberculosis, for the most part in older people. The 1951 report of the Bureau of Crippled Children (6) showed that, in the entire Territory, there were only 12 cases of bone and joint tuberculosis in persons under the age of twenty listed, with an additional 23 showing "late effects of bone and joint tuberculosis." Although real proof is lacking, it would seem that the elimination of bovine tuberculosis accounts to a considerable extent for this change in the incidence of certain forms of nonpulmonary tuberculosis.

Although his name is all but lost in obscurity, the able Dr. Norgaard is deserving of the highest tribute for making one of the greatest contributions to tuberculosis control in Hawaii.

Control program of the Tuberculosis Bureau: Upon its establishment in 1910, the Tuberculosis Bureau was confronted with a tremendous problem but it set to work with a grim determination which has characterized it ever since. The earliest efforts were directed to case reporting and education. In both instances, the gains for some years were exasperatingly slow and meager. Such cases as were reported were, to a large extent, reported after death or when the disease was in a far advanced state.

The year 1922 saw the establishment of the Honolulu Chest Clinic at the Bureau of Tuberculosis and, shortly thereafter, similar diagnostic clinics were in operation on the outer Islands under the direction of the sanatorium medical directors. The latter clinics have continued to carry on diagnostic and case-finding activities and to provide for careful follow-up of the patients discharged from their sanatoriums. A local register is maintained on each of these Islands in addition to the central register in Honolulu. The director of the Bureau of

Tuberculosis cooperates with, and assists in, the control program on the outer Islands.

Commencing with Stewart Doolittle's tuberculin and roentgenographic survey of a large junior high school in Honolulu in 1929 (32), increasing emphasis was given to active search for new cases. Through the succeeding years up to 1940, there was an increasing application of tuberculin surveys with fluoroscopic or roentgenographic examination of positive reactors in clinic contacts, schools, industries, and institutions.

In 1940, following Bruce Douglas's study in Hawaii (33), a new method was introduced, namely, the use of roentgenographic survey without prior skin testing. The first large-scale application, opening the way to its extensive use in succeeding years, was the examination of draftees. Hawaii was probably one of the earliest United States communities to obtain roentgenograms on all of its draftees. By June, 1942, some 12,000 draftees had been examined, roughly 2.8 per cent from urban areas and 1.4 per cent from rural areas showing evidence of tuberculosis. During the next two years, with the acquisition of a mobile unit, the program was greatly accelerated with surveys of civilian war workers, private industries, low economic groups, schoolteachers, and food handlers. Observations at Leahi Hospital directed attention to the exceptionally high incidence of tuberculosis in this latter group. Beginning with the survey of 10,000 food handlers in Honolulu in 1943 (34), when 300 persons were found to have characteristic lesions, a new Board of Health regulation was adopted which has required an annual chest roentgenogram of all food handlers.

In succeeding years there has been continued relentless application of miniature roentgenographic examination of large segments of the population throughout the Islands. Without going into detail, it may be pointed out that considerably more than 60 per cent of the population, aged fifteen or older, have had one or more chest roentgenograms. For the Islands, other than Oahu, this figure exceeds 80 per cent and, in one instance, has reached 96 per cent. In addition to periodic mass roentgenographic surveys, such as that of 1947 in Honolulu when 92,000 were examined (approximately 50 per cent in the city over the age of fifteen), certain groups have had regular annual roentgenograms. The latter included, in addition to food handlers, schoolteachers, and many industries, high school and university students. That there has been no retrenchment in the program is shown by the Tuberculosis Bureau figures (6), which show 120,000 persons examined roentgenographically in 1951 and 127,000 in 1952. As might be expected, the number of cases of reinfection disease detected has been dropping, as shown by Schlosser (35) (1.65 to 0.7 per cent from 1945–1946 to 1949). In 1951, 49.4 per cent of reinfection and suspect cases detected were already on the Tuberculosis Bureau register.

It is quite evident that the Tuberculosis Bureau in Hawaii is carrying on a most outstanding program which can be matched by few communities anywhere. The effect of this work is already evident, and it requires but little imagination to appreciate what a tremendous influence it is destined to have on the tuberculosis picture in the next decade or two.

Isolation and treatment: There are four tuberculosis hospitals in Hawaii and they too have played an immensely important part in controlling the disease. The first of these to be established was Leahi Hospital in Honolulu, which originated as a "Home for Incurables" following upon the heels of the plague epidemic. In 1951, it celebrated its fiftieth anniversary, one of the oldest tuberculosis institutions west of the Rockies. Kula Sanatorium on the island of Maui was opened in 1910; Puumaile Hospital on Hawaii in 1912; and Samuel Mahelona Memorial Hospital on Kauai in 1917. The outer Island hospitals are under county management in contrast to Leahi Hospital which, although serving as the public tuberculosis hospital in Honolulu, has retained its identity as a private nonprofit corporation operated by a board of trustees. The four hospitals receive their operating funds from the Territorial government. As the result of a recent building program, these hospitals today provide a total of about 1,250 beds for the treatment of all forms of tuberculosis. Additionally, there are approximately 100 beds in Tripler Army Hospital for the care of tuberculosis in military personnel and veterans.

Hitherto, there has never been a sufficient number of beds to meet actual needs despite the fact that the over-all bed capacity for many years has exceeded the standard formula based on beds per death. Authorities on the Islands have long been of the opinion that this formula is quite unrealistic, for Hawaii's needs at least, and, consequently, it has been the aim to provide a truly adequate number of beds. The long-sought goal has finally been attained—a bed for every active case in need of hospitalization. As a result, waiting lists which have existed for many years are practically eliminated.

It would be quite inappropriate in a paper of this nature to describe the facilities and treatment programs of Hawaii's tuberculosis hospitals. Suffice it to say that, in each instance, the facilities are thoroughly modern and the medical and surgical programs comparable with, and in some respects superior to, the average mainland institution. Therapeutic programs during the past half century, in general, have followed the trends and fads of mainland centers, with bed rest as a "sheet anchor" at all times. Collapse therapy in all forms was widely applied for many years but enthusiasm has been most decidedly on the wane in more recent years. Streptomycin was first tried at Leahi Hospital in the latter part of 1946. Subsequently, chemotherapy and resectional surgery have been used extensively, with highly gratifying results.

Leahi Hospital in Honolulu is the largest of the four hospitals. Because of its size, approximately 700 beds, it is obviously in a better position to furnish many services which the smaller hospitals are unable to offer. This, however, in no way detracts from the fact that the smaller institutions are carrying out first-rate programs.

Great emphasis is placed on the importance of auxiliary services to patients, stressing occupational therapy, social service, and rehabilitation. Without doubt these well-developed services account in large measure for a very low rate of irregular discharge. The four hospitals follow their discharged patients with extreme care for prolonged periods. Because of geographical isolation, remarkably few patients are lost from surveillance while they remain in the Territory.

During the past year, for example, only 28 of the total 5,981 registered cases were unlocated. Additionally, Hawaii does not have the problem of transient patients.

Unquestionably, the isolation of a high proportion of persons with known active disease over a period of years has lessened the chances of acquiring infection. In 1930, 61 per cent of the persons with active disease in Honolulu were hospitalized, with even a greater percentage isolated on the outer Islands. The

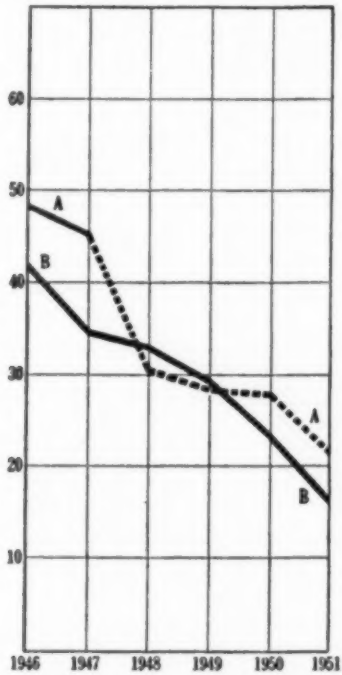

FIG. 6. Percentage of total active reinfection cases and tuberculosis deaths at home in Honolulu during the years 1946–1951.

A-A: Of total active and reinfection cases in City and County of Honolulu, this percentage is at home.

B-B: Of total tuberculosis deaths in City and County of Honolulu, this percentage died at home.

situation in more recent years is shown in figure 6, which gives the percentages of total active reinfection cases and deaths at home in Honolulu from the year 1946 through 1951.

In figure 7 may be seen how the tuberculosis mortality rate per patient per year at Leahi Hospital has declined from 1914 to 1950. It need only be said that this favorable change has resulted, in part, from intensive case finding but, to a much greater extent, from highly effective modern treatment and careful medical follow-up with readmission at the earliest sign of reactivation. The

percentage of patients with far advanced tuberculosis admitted to Leahi Hospital has dropped appreciably in recent years, being 23 per cent in 1952 as compared with 50 per cent or more two decades ago. The strikingly beneficial effects of chemotherapy and resectional surgery on the fate of patients with advanced and

FIG. 7. Tuberculosis mortality rates per patient per year, Leahi Hospital, Honolulu, for the years 1914–1950.

$$\text{Method: } \frac{\text{Yearly tuberculosis deaths}}{\text{Average daily census}} \times 100$$

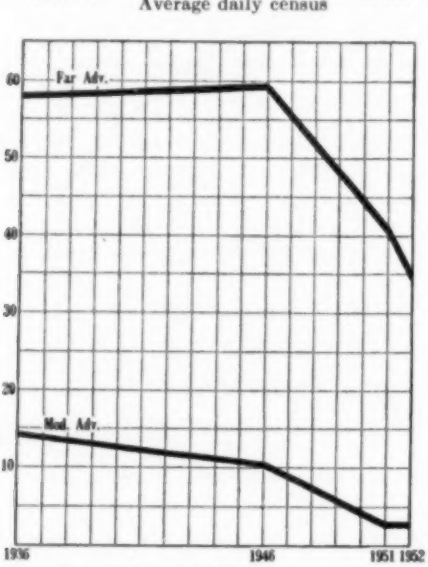

FIG. 8. Percentage of tuberculosis mortality by stage for the years 1936–1952; total tuberculosis patients treated during the year at Leahi Hospital, Honolulu.

moderately advanced disease treated at Leahi Hospital since 1946 is illustrated in figure 8.

Health education: Organized health education began in 1909 with the formation of an Anti-Tuberculosis Committee in Honolulu. The program was well con-

ceived with strong emphasis on free literature and health exhibits. In 1912, Seal Sales entered the picture and were continued until 1917, when the work of the Committee came to an end because of the war. In 1929, Kauai organized its Tuberculosis Association and Seal Sale campaign. The year 1931 saw the beginning of Oahu's Association, which originated as the Palama Tuberculosis Committee. Its first secretary, interestingly enough, was a very young man, James Stone, soon destined to enter bigger fields. In 1932, Maui and Hawaii's associations were organized. These four local units joined together to form a Territorial Association and all are continuing to play an important role in the fields of health education, special studies, assistance to official agencies, case finding, and the financing of new projects. Rehabilitation has been of paramount importance for several years. A most successful workshop for discharged patients is operated by the Oahu Association.

A good measure of the success of the efforts in the control of tuberculosis in Hawaii may be attributed to the work of these voluntary associations. It is frequently difficult to appraise the effectiveness of health education methods. It is the present writer's very decided opinion, however, that the programs conducted by the tuberculosis associations in Hawaii through the years deserve major credit for overcoming ignorance and prejudices among various racial groups.

Public and governmental support: It would be remiss to fail to state that the achievements would have been impossible but for the wholehearted backing and financial support of Hawaii's citizenry and government. By the end of World War II, the Territorial legislature had become convinced of the imperative need for an all-out fight, involving the expenditure of large sums of money, if a substantial gain was to be made. The extent of their cooperation and assistance was truly remarkable. First, in recognition of the need for additional beds and modernization of hospital facilities, the legislature appropriated several million dollars in order to build new hospitals to replace the obsolete facilities at Puumaile and Mahelona Hospitals and to expand the bed capacity of Leahi Hospital and complete the modernization of its inadequate facilities. Second, recognizing that tuberculosis was a public responsibility, they very wisely enacted laws of far-sweeping importance: (*1*) providing for free diagnostic services at the Tuberculosis Bureau; (*2*) instituting a law entitling Hawaii's residents to free care in the four hospitals; and finally, (*3*) a law enabling the Board of Health authorities, when necessary, to commit recalcitrant patients with open disease to a hospital by court action. The Territorial government very liberally provides the operating funds for each hospital to make possibe high standards of medical and surgical treatment. Few nations or states can boast of such overwhelming support from their governments.

GENERAL COMMENT

An attempt has been made to show that Hawaii's energetic tuberculosis control program has gone a long way towards accomplishing what Robert Koch insisted could be achieved by vigorous application of certain basic principles. Certainly, there has been a remarkable reduction in mortality in recent years.

Furthermore, the evidence strongly points to significant changes in morbidity, with respect to age, sex, and race. Within a relatively short time, the disease has assumed greatest importance in older people and is no longer the great killer of infants and children. There is very good reason to assume that the opportunities for acquiring infection have been reduced materially. It would seem, as Sir William Osler might have expressed it, that there are fewer seeds and a stonier ground. Full recognition is given to the influence of improved living conditions, better nutrition, and elimination of adverse environmental factors. However, there can be little doubt that specific measures have been of paramount importance in recent years.

As for the Hawaiians, it has been indicated that they reacted as do all primitive peoples when tuberculosis was first introduced in their midst. The writer's impression has been that the Hawaiians, Samoans, and Filipinos, until very recently at least, manifested an unusual incidence of acute caseopneumonic and generalized forms of the disease, as described by Pinner and Kasper (36) in their pathological studies on American Negroes. However that may be, the fact remains that the Hawaiians, with the coming of the whites, experienced a violent upheaval in their mode of living, and were soon subjected to most unfavorable environmental conditions which, together with spiritual and emotional crises, caused the disease to be excessively prevalent and so acutely fulminating as to kill them off by the thousands.

Unquestionably, tuberculosis was once epidemic amongst the Hawaiians and it would seem that today, the peak having long since passed, it is assuming an endemic form. How the disease would have affected them had they remained in their original state gives cause for speculation. Today, the descendants of those who survived the epidemic of years past, in general, exhibit forms of disease not unlike those found in the other racial groups. Perhaps this indicates that the present generation is beginning to display in some measure an ability to acquire resistance.

What of the future? Belief is strong in the efficacy of the program but it is imperative that it be continued relentlessly for a long time to come. It is believed that retrenchment in any respect would inevitably halt recent progress and perhaps lead to a disastrous setback. The hospital beds will be used for tuberculous patients for several years, if attention is focused on the living registered cases. There is a very real need for a strong educational program by National and local associations to disabuse the general public, health administrations, and legislators of the false notion that mortality reductions and "wonder drugs" spell the end of tuberculosis.

Without question, some aspects of the program should be strengthened. In roentgenographic surveys, greater efforts must be made to search for the hidden foci of disease which are known to be present in the hitherto unreached portion of the population. The minimal lesions discovered by roentgenography always must be considered to have serious potentialities. Hence, they deserve much more careful study by microbiologic methods to determine "activity" with prompt hospitalization and treatment of the patients with active lesions and very careful prolonged observation of the lesions designated as inactive. One of the most

pressing needs in clinical tuberculosis today is an accurate means of determining the "activity" of a lesion. Until the laboratory investigators can provide such a test, the clinician is largely guessing which patient is in need of treatment, how long treatment should be continued, when the patient may be discharged from the hospital, and when he may resume full activity. Certainly, however, a considerable amount of helpful information can be acquired from the careful study of discharged patients. The fate of the discharged patients in Hawaii should be studied more thoroughly, particularly in relation to the effects of chemotherapy and resectional surgery, and with respect to the rehabilitation program.

Finally, the writer believes we are on the threshold of a new era and, following the example set by Myers (37) in Minnesota, should begin to focus more attention on tuberculous infection. It is believed that invaluable information can be gained from extensive application of tuberculin testing, and it is proposed that careful studies be made at various age levels, in various races, in different areas of the Territory. Thinking should be in terms of repeated tuberculin testing of the entire population in the very near future. It is important to know the significance of first infection in adults as compared with children. Furthermore, the writer agrees with Myers (37) and Waring (38) that the time has come when it should be recognized that tuberculous infection means the beginning of disease which all too frequently becomes serious, if not fatal. Accordingly, serious consideration should be given to the treatment of the disease with chemotherapy at the earliest possible moment, as is done in the case of syphilis. Lastly, the effective control program and the valuable role which tuberculin testing is destined to play from now on are sufficient reasons for thinking that the general application of BCG has no place in Hawaii's program, no matter how valuable it may be in the prevention of the disease in other areas.

Acknowledgment

I wish to express my gratitude to Dr. Robert N. Perlstein, Assistant Director, Leahi Hospital, my associate during the past quarter century, for the preparation of the tables and figures, as well as for his valuable suggestions and criticisms.

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ROENTGENOGRAPHIC SPREADS OF PULMONARY TUBERCULOSIS OCCURRING DURING SANATORIUM RESIDENCE BEFORE THE USE OF PROLONGED CHEMOTHERAPY[1, 2]

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INTRODUCTION

Judging from the absence of reports to be found on the subject, little is known about the incidence and causes of roentgenographic spreads of pulmonary tuberculosis during sanatorium residence. Studies of factors related to relapse *after discharge* of different groups of patients (1–5) have focused attention on the problem of spread of disease at the sanatorium. These previous studies suggest that the extent, age, and activity of the disease and the selection and management of collapse therapy are related to *post*-discharge spread.

It has been observed that 20 to 40 per cent of all primary progressions of minimal tuberculosis which occurred between admission and five years after discharge will have occurred before discharge from the sanatorium (3). The purpose of the present study is to determine why and how often progression occurs under the protection of the sanatorium environment.

MATERIALS AND METHODS

The reports of serial chest roentgenograms in the clinical records of all patients admitted to Trudeau Sanatorium between July 1, 1946, and June 30, 1951, were reviewed. Forty-eight of the patients had not been discharged by December 31, 1951; any spreads of disease after this date in these 48 patients were excluded from consideration. This period was selected because it coincided with the writer's personal acquaintance with the patients and because it preceded the routine use of prolonged streptomycin–para-aminosalicylic acid (PAS) therapy.

There were 841 patients admitted with active pulmonary tuberculosis and without major nontuberculous complications during these five years. This number did not include 14 patients whose lesions were classified as inactive at the time of admission. The disease was classified as inactive (*1*) when sputum was negative for acid-fast bacilli and sputum and gastric washings were negative for *M. tuberculosis* on culture; and (*2*) when the abnormal roentgenographic shadows were entirely calcific and/or stringlike. Fifteen were also excluded because of major nontuberculous complications (advanced emphysema, malignant tumor, disseminated lupus erythematosus, diabetes, cardiac decompensation, and pregnancy).

Spread of tuberculosis is defined for the purpose of this investigation as any definite increase in the abnormal shadowing seen on routine stereoscopic chest roentgenograms taken at four- to eight- (usually six) week intervals during the entire sanatorium course. This includes "spreads" at or near the site of previous disease as well as in any previously uninvolved area. The appearance of new areas of rarefaction replacing pre-existing abnormal shadows without any subsequent new shadows was not classified as "spread"; there were 2 such cases. A change in sputum findings from negative to positive for acid-fast bacilli or *M. tuberculosis* without coincident or subsequent increase in roentgenographic shadows

[1] From Trudeau Sanatorium, Trudeau, New York.

[2] This study was aided by a grant from the Committee on Medical Research of the American Trudeau Society, medical section of the National Tuberculosis Association.

also occurred in 5 cases; these were likewise not classified as "spreads." Furthermore, serial chest roentgenograms must have shown improvement or remained unchanged for three months following a "spread" before the case was considered at risk of a second "spread." In other words, consecutive unfavorable films within a three-month limit were classified as a single "spread." Consecutive unfavorable roentgenographic changes were observed within this three-month period in 8 instances.

In all cases in which an actual or possible "spread" was described in the record by any member of the staff, the films were reviewed by the present writer. When the original reading of "spread" was changed to "no spread," this change in interpretation was confirmed by one or more additional observers.

Numerous planigrams and reports of chest fluoroscopy were available on all of the patients in this study. Pertinent amnestic, physical, and laboratory findings were obtained from the records. Evaluation of the emotional status was made by one or more physicians who knew the patient personally, and not by a psychiatrist.

Certain differences in results were tested for statistical significance by chi-square or standard error methods. A difference which would be expected by chance in no more than 2 per cent of the cases was considered significant (*S*). All differences which failed to meet this criterion were rated nonsignificant (*NS*), even though in many cases they may have been indicative of possible or even likely interdependence of the developments being tested.

OBSERVATIONS

Results in All Patients

There were 124 individual "spreads" observed in 112 different patients; 97 patients had one "spread," 9 had two, and 3 had three "spreads" during the study period.

Eighteen "spreads" were discovered on the first check film taken after admission (at four to six weeks). These 18 "spreads" may actually have begun before admission or may at least have been related to treatment or lack of treatment prior to admission.

Eighteen "spreads" were observed within four weeks after a surgical procedure (resection, thoracoplasty, phreniclasis, induction of pneumothorax, and bronchoscopy). It is well recognized, however, that bronchoscopy (6) and surgical interference may not have been the cause of these "spreads."

The extent of "spread" was roughly classified as *mild* (slight increase in abnormal shadows); *marked* (development of a new cavity of 3 cm. or more in diameter, extensive dense shadows, or both); and *moderate* (somewhere between the two extremes). In table 1 it may be seen that there was a tendency toward more extensive "spreads," depending upon the extent of the disease before the "spread." Postoperative "spreads" and those discovered on the first check film were analyzed separately.

Association with new symptoms: The presence and severity of new symptoms coincident with the spread, such as cough, expectoration, wheeze, fever, prostration, hemoptysis, pleurisy, and the like, were significantly greater the more extensive the "spread" (table 2). The 18 postoperative "spreads" were excluded because of uncertainty in ascribing the cause of the new symptoms.

New symptoms, when present, tended to coincide with or precede rather than follow the roentgenographic evidence of "spread."

Seasonal and yearly incidence: The seasonal and yearly incidence of "spreads"

in the five-year period is presented in table 3. In each seasonal column the observed number of "spreads" for a three-month period has been multiplied by four in order to express the results as yearly rates. The problem of varying durations of sanatorium residence is corrected in this table by using the average census of patients with active disease not complicated by serious nontuberculous diseases.

TABLE 1

EXTENT OF SPREAD OF TUBERCULOSIS BY EXTENT OF DISEASE BEFORE SPREAD IN ACTIVE PULMONARY TUBERCULOSIS

EXTENT OF DISEASE BEFORE SPREAD	EXTENT OF SPREAD (NUMBERS)			
	Mild	Moderate	Marked	Total
Minimal	12	8	0	20
Moderately advanced	18	22	6	46
Far advanced	8	11	3	22
	NS			
Spread within four weeks following surgical procedure	5	10	3	18
Spread within four to six weeks after admission	12	6	0	18
Totals	55	57	12	124

NS = Not significant.

TABLE 2

SYMPTOMATOLOGY VERSUS EXTENT OF SPREAD IN ACTIVE PULMONARY TUBERCULOSIS Excluding 18 Postoperative Spreads

EXTENT OF SPREAD	SYMPTOMATOLOGY (NUMBER OF SPREADS)				
	None	Mild	Severe	Total	Per Cent Distribution
Mild	38	10	2	50	47.2
Moderate	12	17	18	47	44.3
Marked	1	3	5	9	8.5
Totals	51	30	25	106	
Per cent distribution	48.1	28.3	23.6	100	100.0
			S		

S = Significant.

Prolonged streptomycin-PAS therapy was not used frequently until mid-1951, except after "spread" had occurred.

The highest incidence of "spread" was in the winter, and lowest in the summer and fall; these seasonal differences were not statistically significant. "Spreads" in 1947 were significantly more frequent than in each later year. Yearly differences were otherwise not remarkable.

It is particularly noteworthy that, in 1952, the yearly incidence of "spreads"

had fallen to 4.6 per cent (6 spreads, with an average census of 130), significantly lower than for the five preceding years. In 1952, streptomycin-PAS therapy was given routinely soon after admission. The only exceptions were a few cases selected for isoniazid or iproniazid therapy.

The incidence of "spread," by extent of disease, age, and sex, and person-years of sanatorium residence is shown in table 4.

Influence of age: Spreads of minimal tuberculosis were more frequent in the 15 to 23-year age group than in those 24 years of age and older, especially in males. Incidence of spread of disease of all extents fell somewhat more with advancing age in females than in males. Incidence of "spread" was otherwise unrelated to sex and seemed not in any way related to extent of disease before spread.

TABLE 3

SEASONAL AND YEARLY INCIDENCE OF SPREADS OF ACTIVE PULMONARY TUBERCULOSIS DURING SANATORIUM RESIDENCE, 1947–1951

YEAR	JANUARY–MARCH		APRIL–JUNE		JULY–SEPTEMBER		OCTOBER–DECEMBER		ENTIRE YEAR	
	Number of Spreads / Average Census	Annual Spread Rate	Number of Spreads / Average Census	Annual Spread Rate	Number of Spreads / Average Census	Annual Spread Rate	Number of Spreads / Average Census	Annual Spread Rate	Number of Spreads / Average Census	Annual Spread Rate
		per cent		*per cent*		*per cent*		*per cent*		*per cent*
1947	9/175	20.6	17/175	38.9	8/187	17.1	8/166	19.3	42/175	24.0
1948	8/153	20.9	8/167	19.2	5/188	10.6	4/172	9.3	25/170	14.7
1949	6/168	14.3	2/164	4.9	4/179	8.9	5/166	12.0	17/169	10.1
1950	6/163	14.7	6/159	15.1	4/170	9.4	4/149	10.7	20/160	12.5
1951	9/141	25.3	3/147	8.2	6/161	14.9	3/131	9.2	21/145	14.5
Mean	7.6/160	19.0	7.2/162	17.8	5.4/177	12.2	4.8/157	12.2	25/164	15.2
						NS				

NS = Not significant.

Miscellaneous findings: The following observations are presented without supporting numerical data, none of the differences being statistically significant. "Spreads" tended to be more extensive in the presence of cavity than in its absence. Extent of "spread" was not shown to be related to the bronchoscopic findings in 96 cases. Incidence and extent of "spread" were not shown to be related to a history of previous short courses (42 to 120 days) of streptomycin or streptomycin-PAS in 136 cases, nor to the level of physical activity which had been prescribed for the patient at the time of the "spread." Information on unprescribed activity was not available.

"Spreads" were more apt to be unilateral than bilateral, local than distant. "Spreads" to distant uninvolved parts of the lung were more common in the presence than in the absence of cavity or active endobronchial disease, and understandably were more common before the ambulant stage of treatment had been reached.

In approximately one-third of the "spreads," an insidious increase of shadowing was observed, often only in retrospect, during the six to twelve weeks before "spread" occurred.

Twenty of the "spreads" occurred within three weeks after a leave of absence of seven days or more, while 8 additional "spreads" followed leaves of one to seven days. Needless to say, there were many leaves of absence not followed by "spread."

TABLE 4

INCIDENCE OF SPREADS OF ACTIVE PULMONARY TUBERCULOSIS PER PERSON-YEARS IN THE SANATORIUM BY EXTENT OF DISEASE, AGE, AND SEX

NTA CLASSIFICATION	AGE	MALE				FEMALE				BOTH SEXES			
		Persons	Person-Years at Risk	Spread		Persons	Person-Years at Risk	Spread		Persons	Person-Years at Risk	Spread	
				Number	Per cent			Number	Per cent			Number	Per cent
Minimal	15–23	24	19.4	5	25.8	58	54.5	13	23.9	82	73.9	18	24.4
	24–33	48	29.3	0	0	60	44.5	4	9.0	108	73.8	4	5.4
	34+	17	10.3	0	0	21	12.5	3	24.0	38	22.8	3	13.2
	Total	89	59.0	5	8.5	139	111.5	20	17.9	228	170.5	25	14.7
Moderately advanced	15–23	107	98.6	12	12.2	65	78.6	12	15.3	172	177.2	24	13.5
	24–33	120	104.6	13	12.4	116	134.0	21	15.6	236	238.6	34	14.3
	34+	34	23.2	3	12.9	48	52.2	3	5.8	82	75.4	6	8.1
	Total	261	226.4	28	12.4	229	264.8	36	13.6	490	491.2	64	13.0
Far advanced	15–23	33	47.1	11	23.4	16	26.8	5	18.7	49	73.9	16	21.6
	24–33	29	50.7	6	11.8	24	42.9	9	21.0	53	93.6	15	16.1
	34+	12	21.3	3	14.1	9	17.5	1	5.7	21	38.8	4	10.3
	Total	74	119.1	20	16.8	49	87.2	15	17.2	123	206.3	35	17.0
All extents	15–23	164	165.1	28	17.0	139	159.9	30	18.8	303	325.0	58	17.8
	24–33	197	184.6	19	10.3	200	221.4	34	15.4	397	406.0	53	13.1
	34+	63	54.8	6	10.9	78	82.2	7	8.5	141	137.0	13	9.5
	Total	424	404.5	53	13.2	417	463.5	71	15.3	841	868.0	124	14.3

Fifteen "spreads" occurred on films taken immediately prior to a planned discharge. Five of the 15 occurred in patients with minimal, and 10 in patients with moderately advanced, disease. Sputum smears were negative for acid-fast bacilli in each case, and in only 2 were cultures intermittently positive for *M. tuberculosis* in the two months preceding the "spread." Ten of the 15 had had three or more negative cultures during the two months before "spread." The extent of "spread" was mild in 10, moderate in 4, and marked in one. The "spread" was distant in 2 and local in 13. Five had had insidious increases in disease just before "spread," in retrospect; 10 had not. It was remarkable that all occurred

in young women between the ages of 20 and 32 (mean: 24); all were single except 3, one of whom was recently divorced and one unhappily married. Severe emotional problems had been recognized before "spread" in 7. In 3, there was some evidence of a subconscious desire to remain within the "security" of the sanatorium environment.

Results in Minimal Tuberculosis

The age of a minimal lesion was determined whenever possible. A patient with a negative chest film or a negative tuberculin test within eighteen months prior to admission was classified as having "newly acquired" disease. Patients who were under treatment for reactivation of a lesion seen on a chest film eighteen months or more before admission were classified as having "old" disease. In all others, age of disease was classified as undetermined. The results of this analysis (table 5) were inconclusive, especially since the "spread" rate was lower in those with undetermined age of disease than in either of the known groups.

TABLE 5

RELATIONSHIP OF AGE OF DISEASE TO INCIDENCE OF SPREAD OF ACTIVE MINIMAL PULMONARY TUBERCULOSIS BY PERSON-YEARS AT THE SANATORIUM

AGE OF DISEASE	PERSONS	PERSON-YEARS AT SANATORIUM	SPREAD	
			Number	Per Cent
"Newly acquired"	79	64.9	9	13.9
"Old"	73	52.0	10	19.2
Undetermined	76	53.6	6	11.2
Total	228	170.5	25	14.7
				NS

NS = Not significant.

Relation of bacteriologic findings: The patients with minimal disease were classified by their sputum bacteriologic findings. A patient classified as "positive" had one or more positive findings before "spread" in those with "spread," or before discharge in the balance.

Patients with positive smear were observed to be no more apt to have "spread" than those with negative smear (table 6).

The difference in "spread" rate between patients classified as positive and negative by culture was not statistically significant (table 7); the figures were interesting, however, since there was a small difference in the *opposite* direction when the patients were classified by the sputum-smear findings.

Emotional factors: An earnest attempt was made to determine the relationship, if any, of spread of minimal disease to emotional factors. The 228 patients with minimal tuberculosis were classified as (*1*) ostensibly normal or average; (*2*) emotionally disturbed but not disabled by anxiety; (*3*) frankly psychoneurotic; (*4*) adult behavior problems or psychopathic personalities; and (*5*) undetermined. Ninety-one patients fell into the last-named classification. There was no demon-

strable relationship between the patients so classified and the incidence of "spread."

Influence of type of rest regimen: Certain of the patients with minimal disease were admitted to infirmary care, while the balance were admitted to a less

TABLE 6

RELATIONSHIP OF SPUTUM BACTERIOLOGY TO INCIDENCE OF SPREAD OF ACTIVE MINIMAL PULMONARY TUBERCULOSIS BY PERSON-YEARS AT THE SANATORIUM

SPUTUM BACTERIOLOGY*	PERSONS	PERSON-YEARS AT SANATORIUM	SPREAD	
			Number	Per Cent
Smear positive				
Culture positive or no culture†	24	25.7	3	11.7
Culture negative	13	9.2	1	10.9
Smear negative or no smear				
Culture positive	37	32.9	9	27.4
Culture negative	147	100.4	12	12.0
No culture	7	2.3	0	0
Total	228	170.5	25	14.7

* All smears were 50-hour concentrates; cultures were 50-hour concentrates if sputum was available, otherwise gastric washings.

† Previous sanatorium policy of not routinely making cultures on smear-positive cases is responsible for there being no cultures obtained in 12 cases. A smear was usually made at monthly intervals in all cases, and three gastric washing cultures were made at two or three monthly intervals in smear- and culture-negative cases.

TABLE 7

RELATIONSHIP OF SPUTUM SMEAR VERSUS SPUTUM AND/OR GASTRIC WASHING CULTURE FINDINGS TO INCIDENCE OF SPREAD OF ACTIVE MINIMAL PULMONARY TUBERCULOSIS BY PERSON-YEARS AT THE SANATORIUM

BACTERIOLOGY	SPUTUM SMEAR				SPUTUM OR GASTRIC WASHING CULTURES			
	Persons	Person-Years at Sanatorium	Spread		Persons	Person-Years at Sanatorium	Spread	
			Number	Per cent			Number	Per Cent
Positive	37	34.9	4	11.5	56	54.6	12	22.0
Negative	155	111.2	16	14.4	160	109.6	13	11.9
Total	192*			NS	216†			NS

* No sputum was available in 36.

† No cultures were obtained in 12.

NS = Not significant.

stringent regimen in a "rest cottage," described as modified bed rest. Modified bed rest is defined as approximately twenty to twenty-one hours per day reclining in bed or on a chaise longue, with meals eaten in an adjoining room and full bathroom privileges. Riding or walking to other buildings for necessary examinations was permitted. Patients admitted to infirmary care were given

fewer privileges, twenty-two to twenty-three hours per day in bed, and considerably more supervision. Treated first in one way and then in the other, most patients have reported that the rest cottage environment is more conducive to rest than the infirmary, especially after initial indoctrination in the infirmary.

After one to five months, patients admitted to the infirmary with minimal tuberculosis were promoted to the rest cottages. Those who remained in the sanatorium long enough graduated from the rest cottage to formal out-of-door exercise. The average duration of bed rest (infirmary plus rest cottage or rest cottage only) and sanatorium residence was approximately the same in these two groups which were distinguished only by the regimen prescribed on admission. In certain instances clinically sick patients were admitted to the infirmary

TABLE 8

CUMULATIVE YEARLY RATES OF SPREAD OF MINIMAL PULMONARY TUBERCULOSIS FOR THE FIRST FIFTEEN MONTHS OF SANATORIUM RESIDENCE BY TYPE OF REST PRESCRIBED ON ADMISSION (LIFE TABLE)

MONTHS AFTER ADMISSION	ADMISSION INFIRMARY		ADMISSION COTTAGE		ALL CASES	
	Cases at Risk	Cumulative Spread Rate per Year	Cases at Risk	Cumulative Spread Rate per Year	Cases at Risk	Cumulative Spread Rate per Year
1	60	1.7	174	1.2	234	1.3
2	59	1.7	172	3.6	231	3.1
3	58	5.1	159	6.7	217	6.3
4	52	5.1	142	8.0	194	7.2
5	48	5.1	124	8.0	172	7.2
6	46	5.1	105	8.9	151	7.8
7	42	5.1	89	12.0	131	9.9
8	37	7.7	69	14.5	106	12.5
9	31	10.7	51	14.5	82	13.5
10	25	*10.7**	32	*17.2**	57	15.0
11	18	10.7	20	17.2	38	15.0
12	16	10.7	14	17.2	30	15.0
15	9	17.3	12	24.4	21	22.2

* Not significant.

in preference to the cottage; more commonly, however, infirmary care was given initially because it was requested by the referring physician.

Incidence of "spread" by months at the sanatorium for the two groups of patients with minimal tuberculosis was computed by life table (table 8) and shows lower rate of "spread" in those given more supervision, not necessarily more rest, initially.

The amount of rest taken is also related to the degree of adherence to the prescribed regimen. Attempts to classify patients in retrospect by this important yardstick were considered unreliable.

COMMENT

In undertaking this investigation it was hoped that some light would be thrown on the incidence, cause, and prevention of spreads of pulmonary tubercu-

losis during sanatorium residence. Only a limited amount of useful information has been forthcoming.

Spreads of tuberculosis were somewhat more common in the 15- to 23-year age group than in those 24 years of age and older. Experience with patients younger than 15 and older than approximately 45 was not available.

The incidence of spread of minimal tuberculosis was more in line with sputum culture than with sputum smear findings. Patients with minimal tuberculosis admitted to infirmary care were apparently less apt to have a "spread" than those admitted to the rest cottage. The factors which may have influenced allocation of these cases on admission did not appear to weight either of these two groups unduly. The rest regimen in the infirmary, while not strict, was somewhat more stringent and definitely more supervised than the modified bed rest regimen in the cottages. The principal differences between the two methods of treatment were round-the-clock nursing service and daily visits by the doctor in the infirmary as against two nursing visits daily and one to two doctor's visits weekly in the cottage. It is believed that more effective education or indoctrination about tuberculosis and its treatment was accomplished in those patients who spent at least their first four to eight weeks in close contact with both doctors and nurses.

The use of 30- to 120-day courses of streptomycin or streptomycin-PAS had no apparent effect on the incidence and extent of subsequent "spread." However, coincident with the routine use of prolonged (nine to twenty-four months) uninterrupted streptomycin-PAS and occasional use of isonicotinic acid hydrazide regimens, the yearly incidence of "spreads" at Trudeau Sanatorium fell from 15.2 per cent in the 1947–1951 period to 4.6 per cent in 1952. In addition, this change occurred in spite of the fact that some patients had had interrupted or inadequate chemotherapy before admission, and streptomycin-resistant and/or PAS-resistant tubercle bacilli were occasionally isolated from sputum on admission.

Attempts to study the influence of emotional factors on "spread" were considered both inadequate and unreliable. There was an impression, however, of a lack of correlation between the known emotional factors and incidence of "spread."

SUMMARY

For five years prior to the routine use of prolonged streptomycin–para-aminosalicylic acid (PAS) therapy at Trudeau Sanatorium, there was about one chance in seven of spread of active pulmonary tuberculosis, without major nontuberculous complications, for each twelve months of sanatorium residence.

The routine use of prolonged uninterrupted streptomycin-PAS therapy was accompanied by an impressive reduction in the incidence of spread of pulmonary tuberculosis during sanatorium residence.

Spread of pulmonary tuberculosis in the sanatorium was no more apt to occur in advanced than in minimal disease.

In patients with minimal pulmonary tuberculosis, "spreads" were more common in the 15- to 23-year age group than in those 24 to 45, particularly in

males. Age and sex had no other demonstrable relationship to incidence of spread of disease, irrespective of its extent.

The behavior of minimal pulmonary tuberculosis in the sanatorium may be more reliably predicted from the findings on culture of sputum or gastric washings than from examination of sputum smears.

SUMARIO

Diseminaciones de la Tuberculosis Pulmonar Observadas Roentgenográficamente Durante la Residencia en el Sanatorio Antes del Empleo de la Quimioterapia Prolongada

Durante los cinco años anteriores al empleo sistemático de la terapéutica prolongada con estreptomicina-ácido para-aminosalicílico (PAS) en el Sanatorio Trudeau, hubo aproximadamente una certeza por siete posibilidades de propagación de tuberculosis pulmonar activa, sin mayores complicaciones no tuberculosas, por cada doce meses de permanencia en el sanatorio.

El empleo sistemático de la continua y prolongada terapéutica con estreptomicina y PAS ha ido acompañada de una reducción imponente de la incidencia de la propagación de la tuberculosis pulmonar durante la estancia en el sanatorio.

La propagación de la tuberculosis pulmonar en el sanatorio *no* fué más susceptible de ocurrir en la enfermedad avanzada que en la mínima.

En los enfermos con tuberculosis pulmonar mínima, las propagaciones fueron más frecuentes en el grupo de 15 a 23 años de edad que en los de 24 a 25, sobre todo en los varones. La edad y el sexo no guardaron ninguna otra relación demostrable con la incidencia de la propagación en todas las formas de la dolencia.

El comportamiento de la tuberculosis pulmonar mínima en el sanatorio puede predecirse más certeramente con los hallazgos bacteriológicos por los *cultivos* del esputo y del lavado gástrico que por los *frotes* del esputo.

RESUME

Extension de la tuberculose pulmonaire révélée par la radiographie au cours du séjour en sanatorium, avant l'emploi de la chimiothérapie prolongée

Pendant cinq années précédant l'emploi routinier du traitement prolongé par l'association streptomycine- para-aminosalicylique (PAS) au Sanatorium Trudeau, il y avait approximativement une chance sur sept d'observer une extension de la tuberculose pulmonaire active, sans complications majeures de la tuberculose, pour chaque cure sanatoriale de douze mois.

L'emploi habituel d'une cure prolongée et ininterrompue streptomycine-PAS s'est accompagné d'une réduction impressionante de l'incidence de l'extension de la tuberculose pulmonaire au cours du séjour en sanatorium.

L'extension de la tuberculose pulmonaire pendant la cure sanatoriale n'était *pas plus* apte à se produire dans les cas avancés que dans les lésions *a minima*.

Chez les malades atteints de tuberculose *a minima* l'extension des lésions ne s'est pas montrée plus fréquente dans le groupe d'âge 15–23 ans que dans celui de 24–25 ans, en particulier chez les hommes. L'âge et le sexe ne présentaient aucune autre relation démontrable quant à l'incidence de l'extension des lésions à tous les stades de la maladie.

Le comportement de la tuberculose pulmonaire *a minima* en sanatorium peut plus vraisemblablement être prévu par les résultats bactériologiques *de la culture* des crachats et des prélèvements par lavage gastrique que par l'*examen direct* du crachat sur lame.

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TOTAL SURGICAL STATISTICS IN THE TREATMENT OF PULMONARY TUBERCULOSIS[1, 2]

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Introduction

The thesis of this paper is that the end results of the total surgical program applied in the treatment of tuberculous patients represent the only surgical statistics of significance; that the true measure of success is not what is accomplished with any one surgical procedure but rather the results obtained using all of the available procedures to salvage the greatest possible percentage of patients who need surgical treatment to get well. The type of case accepted for surgical treatment and the percentage of patients returned to productive living are the two fundamental factors determining the success of any surgical program.

The purpose of this paper is to present and analyze the results of all surgical procedures (phrenics, pneumothorax, and pneumoperitoneum excluded) performed at the Rhode Island State Sanatorium between January 1, 1947, and January 1, 1952 (the streptomycin era). Only those patients in whom surgery was used in an attempt to control parenchymal disease are included. Collapse procedures following resection or to obliterate pleural or extrapleural spaces are not included. The results of each operative procedure used in treating unilateral surgical problems will be analyzed separately. The total results for all cases subjected to unilateral and bilateral surgery will be given. Finally, the end results for the entire group will be presented.

The end results consist of an evaluation of the status of these patients in August, 1952. Thus, a minimum follow-up period of six months and a maximum of five and one-half years are represented. Only 3 patients have been lost from adequate follow-up study.

During this five-year period, 289 patients were accepted for surgical treatment of parenchymal disease. Two hundred and fifty-five of these were considered to have unilateral surgical problems, 4 of which eventually required bilateral treatment. Thirty-four additional patients were considered to have bilateral surgical problems when accepted for surgery.

Definition of Terms

Unilateral surgical problem: A patient with disease considered to require surgery on only one side when accepted. A high percentage had bilateral disease.

Bilateral surgical problem: This term is used to designate patients in whom bilateral surgical procedures were considered necessary to control the parenchymal lesion. The term does not mean merely bilateral disease.

[1] From the Rhode Island State Sanatorium, Wallum Lake, Rhode Island.

[2] Presented before the Medical Session, as part of the session on *Surgery in the Treatment of Tuberculosis*, at the annual meeting of the National Tuberculosis Association, Los Angeles, California, on May 19, 1953.

Sputum negative for tubercle bacilli: In reporting "conversion" rates following surgery, a "negative sputum" indicates that the sputum was consistently negative for tubercle bacilli by both direct and concentrated smear methods and by either culture, guinea pig inoculation, or both. This is true in the cases of all except 10 per cent of the patients who left the sanatorium against advice before the culture or guinea pig studies could be performed. In their cases, the patient's follow-up study must indicate a "negative sputum" status. Otherwise, it is recorded as positive for tubercle bacilli.

Follow-up classification: In the follow-up study, the living patients are classified into four categories:

(*1*) Clinically well with "negative sputum"
(*2*) "Positive sputum" or unstable roentgenogram (salvable cases)
(*3*) Active or progressive disease or respiratory cripple (hopeless cases)
(*4*) Inadequate follow-up (3 patients all known to be living)

Patients are classified according to the opinion of the physician or clinic now caring for them.

Postoperative period: The postoperative period has been set arbitrarily at sixty days. Complications and deaths occurring within this period are listed as postoperative; those occurring after sixty days, as late.

Observations

UNILATERAL SURGICAL PROBLEMS

The surgical program used in treating the 255 patients classified as unilateral problems is given in table 1. A collapse therapy procedure was chosen as the primary surgical approach in 183 cases. In 29 of these, secondary operations were subsequently performed as listed in the table. Four eventually required bilateral surgery. The end results of these 183 cases are the cumulative results of all procedures. Eighty-seven resections were performed.[3]

Figure 1 depicts graphically the changing trends during this five-year period in the surgical approach to treatment. It shows the decline in use of conventional thoracoplasty and the increasing use of plombage thoracoplasty and resection. This is a reflection of the influence of the antimicrobial drugs. In the first two years of this study, para-aminosalicylic acid was not available and only short courses of streptomycin were being used, a very inadequate regimen according to present concepts. In addition, streptomycin was reserved in those days largely for resections. Most of the thoracoplasties were performed without streptomycin preparation or coverage. Only the substandard risks received streptomycin. In recent years, prolonged intermittent therapy with the drugs has extended coverage to the majority of surgical patients. It should also be emphasized that in 1947 and 1948, when resection was being used so little, selection of cases was entirely different than at the present time. At that time, many thoracoplasties were performed for lesions now generally accepted as presenting indications for resection. These factors must be considered when evaluating the results of various surgical procedures.

[3] Two cavernostomies were performed without a concomitant thoracoplasty. Both patients presented rather hopeless problems, and both of them have since died. They are not included in the tables and discussion of this paper.

TABLE 1

UNILATERAL SURGICAL PROBLEMS—255 CASES

Rhode Island State Sanatorium—January, 1947, to January, 1952

TYPE	NUMBER	REMARKS
Collapse Therapy Procedures		
Conventional thoracoplasty (2 with cavernostomy)	93	29 of these patients subsequently had secondary operations:
Extraperiosteal plombage thoracoplasty	68	Resection, 19
Extrapleural plombage thoracoplasty	17	Revision thoracoplasty, 4
Extrapleural pneumothorax	4	Extrapleural plombage, 5
Revision thoracoplasty	1	Cavernostomy, 1
Total	183	
Resection		
Pneumonectomy	49	15 of this group represent collapse therapy failures
Lobectomy	29	
Lobectomy (segmental)	3	
Segmental resection	4	
Wedge resection	2	
Total	87	

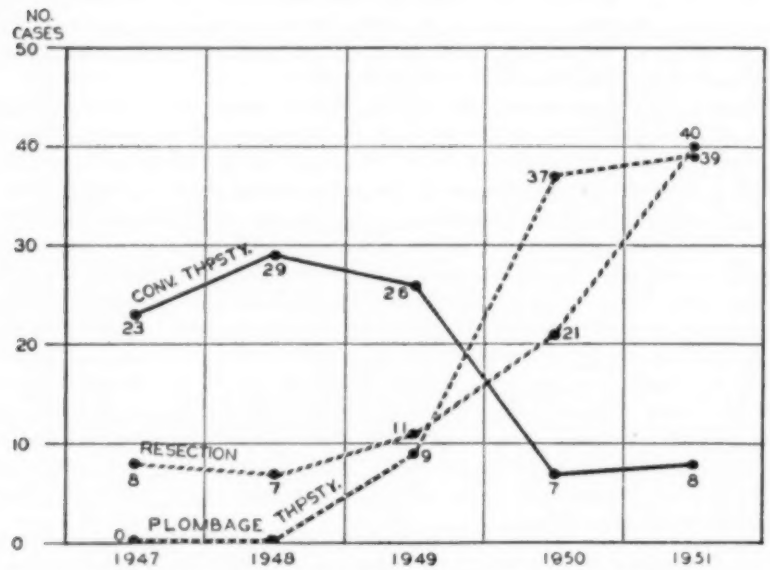

FIG. 1. A graph of the unilateral surgical problems at Rhode Island State Sanatorium, January, 1947, to January, 1952, showing the changing trends in the surgical approach to treatment of pulmonary tuberculosis.

Collapse therapy procedures: The important data concerning the collapse therapy procedures used are presented in table 2. This table is considered to be self-explanatory, and no attempt will be made to analyze it in detail. The following comments may be helpful in interpreting the results:

Primary conversion: The term "primary conversion" designates "conversion" of sputum with the first surgical procedure. "Secondary conversion" means the sputum "converted" only after further surgery. The final "conversion" rate is the sum of the two.

Conventional thoracoplasty: With conventional thoracoplasty, the "conversion" rate is lower and tuberculous complications and death rates are higher than with other procedures. This must not be interpreted to mean that conventional thoracoplasty is an inferior and more dangerous operation. It merely reflects the fact that more conventional thoracoplasties were performed in the earlier years of this study, when case selection was poorer and the use of antimicrobial drugs less efficient.

Secondary surgical procedures: Twenty-nine of the 183 patients subsequently had secondary surgical procedures which resulted in successful "conversion" of the sputum in 26 cases. One death resulted from a secondary operation (lobectomy).

Tuberculous complications: Fifteen of the eighteen tuberculous complications occurred in the conventional thoracoplasty group. In the 90 patients subjected to other collapse therapy procedures, only 3 patients (3.3 per cent) have suffered a tuberculous complication. These procedures have all been performed in the last three years.

The postoperative tuberculous complications were: ipsolateral spread, 5; contralateral spread, one; contralateral exacerbation, one; wound infection, one; bronchopleural fistula following extrapleural plombage, one.

The late tuberculous complications were: contralateral exacerbation, 4; tuberculous bronchitis, 3; recurrence of sputum positive for tubercle bacilli, one; meningitis, one.

Deaths: There were 2 postoperative deaths among the 93 patients treated by conventional thoracoplasty, one caused by coronary arterial thrombosis and myocardial failure and the other by pulmonary insufficiency. There were no postoperative deaths among the 90 patients subjected to the other collapse therapy procedures.

The 6 late deaths in the conventional thoracoplasty group were caused by tuberculous infection in 4 patients and nontuberculous causes in 2 as follows: progressive tuberculosis, 3; meningitis, one; pulmonary insufficiency, 2 (following lobectomy in one case and following extrapleural plombage in the contralateral side in one). The 2 late deaths in the extraperiosteal plombage group were caused by metastatic carcinoma (breast) and coronary arterial thrombosis.

All deaths are included, whether due to the primary procedure or the secondary surgery.

Status of living patients: There is little, if any, significant difference among the various groups in the percentage of patients who are clinically well with sputum negative for tubercle bacilli. This is a reflection of a clinical fact that to date no group of patients has withstood the test of time so well as those whose disease has been controlled by permanent collapse. In this entire group of 183 patients, in only one instance has there been a recurrence of "positive" sputum in the patients who were discharged with medical consent. Only 4 other patients have required readmission because of recurrence of a "positive" sputum originating on the side of surgery;

and one, because of a contralateral exacerbation. These 5 patients all left the sanatorium against advice within a few months of their collapse therapy.

TABLE 2

UNILATERAL SURGICAL PROBLEMS—COLLAPSE THERAPY PROCEDURES
Rhode Island State Sanatorium—January, 1947, to January, 1952

	CONVENTIONAL THORACOPLASTY	EXTRAPERIOSTEAL PLOMBAGE THORACOPLASTY	EXTRAPLEURAL PLOMBAGE THORACOPLASTY	EXTRAPLEURAL PNEUMOTHORAX	REVISION THORACOPLASTY	TOTALS
Number of cases	93	68	17	4	1	183
Results						
Primary "sputum conversion"	63 (68%)	52 (76%)	14 (82%)	3 (75%)	1 (100%)	133 (73%)
Secondary "sputum conversion"	14 (15%)	10 (15%)	1 (6%)	1 (25%)	0	26 (14%)
Final "conversion"	77 (83%)	62 (91%)	15 (88%)	4 (100%)	1 (100%)	159 (87%)
Tuberculous complications						
Postoperative	8 (8.6%)	0	1 (5.9%)	0	0	9 (5%)
Late	7 (7.5%)	2 (2.9%)	0	0	0	9 (5%)
Deaths						
Postoperative	2 (2.2%)	0	0	0	0	2 (1.1%)
Late	6 (6.5%)	2 (2.9%)	0	0	0	8 (4.4%)
Living (August, 1952)	85 (91%)	66 (97%)	17 (100%)	4 (100%)	1 (100%)	173 (94.5%)
Well with sputum negative for tubercle bacilli	75 (88%)	60 (91%)	15 (88%)	4 (100%)	1 (100%)	155 (90%)
Salvable	5 (6%)	5 (7%)	2 (12%)	0	0	12 (7%)
Hopelessly ill	3 (3.5%)	0	0	0	0	3 (2%)
Inadequate follow-up	2 (2.3%)	1 (1.5%)	0	0	0	3 (2%)

Final results: One hundred and eighty-three patients were originally selected for collapse therapy procedures. The postoperative death rate was 1.1 per cent; the late death rate, 4.4 per cent. The final death rate of 5.5 per cent represents

all deaths, whether due to the primary surgical procedure, secondary surgery, or to tuberculous disease. One hundred and seventy-three patients (94.5 per cent) are living and 155 (90 per cent) of them are clinically well with sputum negative for tubercle bacilli. Three patients are living, but the data for classification are inadequate. Of the remaining 15 patients, 12 are clinically well but either have sputum positive for tubercle bacilli or an unstable lesion on serial roentgenograms. These are considered to be salvable cases. Three patients are hopelessly ill at the present time.

Resection: Eighty-seven pulmonary resections were performed. Fifteen of these represent thoracoplasty failures from the collapse therapy series.

Tuberculous complications: Complications occurred in 15 patients (31 per cent) following pneumonectomy, 7 in the postoperative period and 10 late. The postoperative complications were: fistula and empyema, 2 cases; wound infection, 2; wound sinus, 2; contralateral exacerbation, one; contralateral pleural effusion, one; and leukemoid metaplasia considered to be the result of tuberculosis of the bone marrow, one case. The late complications were: stump ulcer, 4 cases; fistula, one; empyema, 3; and contralateral exacerbation, 2 cases.

Following lobectomy, tuberculous complications occurred in 5 patients. The 2 postoperative complications were: fistula and empyema, one case; and contralateral exacerbation, one case. Two stump ulcers and one contralateral exacerbation occurred late.

Fistula and empyema occurred in one of the 3 patients subjected to lobectomy plus segmental resection, and ipsolateral exacerbation occurred in one of the 4 patients who had segmental resections.

Deaths: There were 2 postoperative deaths. One which followed lobectomy was due to pulmonary insufficiency. The other death, which occurred following pneumonectomy, was caused by pulmonary edema which occurred two and one-half hours following operation when a second flask of saline was inadvertently given in its entirety while restarting a transfusion.

The 4 late deaths in the pneumonectomy series were caused by: right heart failure during an attack of viral pneumonia; coronary arterial thrombosis; progressive tuberculosis resulting from fistula and empyema; and leukemoid metaplasia, which in the opinion of the hematologist was secondary to tuberculosis of the bone marrow although this was never proved.

The late death in the lobectomy-plus-segmental-resection group was caused by a fatal hemorrhage from the empyema space. This occurred following the use of streptokinase and streptodornase, and the relation of enzyme therapy may or may not have been coincidental. The late death following segmental resection was due to progression of a postoperative exacerbation of disease.

Final results: Of 87 patients treated by resection, 22 suffered either a postoperative complication, a late complication, or both. Most of these were adequately controlled by further treatment as evidenced by the favorable status of the living patients.

Two deaths (2.3 per cent) occurred in the postoperative period, both due to nontuberculous causes. Six deaths occurred late, 3 due to nontuberculous causes and 3 to tuberculous infection. Attention is called to the small percentage

of deaths now occurring following any type of surgery due to tuberculous infection.

Seventy-nine (90.5 per cent) patients are living and, of these, 94 per cent are clinically well with sputum negative for tubercle bacilli, 3 are salvable, and 2 are hopelessly ill.

TABLE 3

UNILATERAL SURGICAL PROBLEMS—PULMONARY RESECTION

Rhode Island State Sanatorium—January, 1947, to January, 1952

	PNEUMONECTOMY	LOBECTOMY	LOBECTOMY PLUS SEGMENTAL	SEGMENTAL RESECTION	WEDGE RESECTION	TOTALS
Number of cases	49	29	3	4	2	87
Tuberculous complications						
Postoperative	7 (14%)	2 (7%)	1 (33%)	1 (25%)	0	11 (13%)
Late	10 (20%)	3 (10%)	0	0	0	13 (15%)
Deaths						
Postoperative	1 (2%)	1 (3.4%)	0	0	0	2 (2.3%)
Late	4 (8.2%)	0	1 (33%)	1 (25%)	0	6 (6.9%)
Living (August, 1952)	44 (89.8%)	28 (96.5%)	2 (67%)	3 (75%)	2 (100%)	79 (90.5%)
Well with sputum negative for tubercle bacilli	42 (96%)	25 (89%)	2 (100%)	3 (100%)	2 (100%)	74 (94%)
Salvable	1 (2%)	2 (7%)	0	0	0	3 (4%)
Hopelessly ill	1 (2%)	1 (4%)	0	0	0	2 (2%)
Inadequate follow-up	0	0	0	0	0	0

Final Results in the Treatment of Unilateral Problems

The final results of treatment of the entire 255 unilateral surgical problems are given in table 4. There were 4 postoperative deaths (1.6 per cent), all due to nontuberculous causes. There were 13 late deaths (5.1 per cent). Seven of the late deaths were caused by tuberculous infection.

Two hundred and thirty-eight patients (93.3 per cent) are living. Of the living patients, 90 per cent are clinically well and have sputum negative for tubercle bacilli; 63 per cent are salvable; 2.1 per cent are hopelessly ill; in 3 cases, the follow-up observations were not sufficiently adequate to permit classification.

The final results are the statistics of significance. They are the true measure of success of this surgical program of treating unilateral surgical problems.

BILATERAL SURGICAL PROBLEMS

Thirty-four patients were accepted for bilateral surgical treatment when first presented in conference. In addition, 4 patients originally accepted for unilateral surgery finally required bilateral treatment (contralateral pneumothorax not included), making a total of 38 cases.

Bilateral surgery has been completed in 28 cases. The combinations of surgical procedures used are listed in table 5. It should be noted that extrapleural procedures, usually Lucite plombage thoracoplasty, have been the most useful tool in this type of case. Extrapleural procedures were used in a total of 23 of the 28 cases and bilaterally in 11. Eighteen (64 per cent) of these 28 patients are clinically well with sputum negative for tubercle bacilli.

TABLE 4

ALL UNILATERAL SURGICAL PROCEDURES—255 CASES

RESULTS AS OF AUGUST, 1952

Rhode Island State Sanatorium—January, 1947, to January, 1952

Postoperative deaths: 4 (1.6%)		
Tuberculous		
Nontuberculous	4	
Late deaths: 13 (5.1%)		
Tuberculous	7	
Nontuberculous	6	
Living: 238 (93.3%)		
Clinically well—sputum negative for tubercle bacilli	215	(90%)
"Positive" sputum or unstable lesion on roentgenography	15	(6.3%)
Active or progressive disease or respiratory cripple	5	(2.1%)
Inadequate follow-up	3	(1.3%)
Follow-up period:		
More than six months		(100%)
More than one year	239	(94%)
More than two years	148	(58%)
More than three years	93	(37%)
More than four years	52	(21%)
More than five years	16	(6%)

Two patients originally accepted for bilateral surgery required only one side to be done, the contralateral lesion coming under control after one side was completed.

In 8 cases, the surgical program was never completed. Two of these patients died postoperatively (cerebral vascular accident, pulmonary insufficiency). Two late deaths were caused by pulmonary insufficiency. The other 4 patients are respiratory cripples. The writers believe that they are open to criticism in these cases for not having performed adequate functional studies prior to surgery.

Of the total of 38 patients in the bilateral group, 20 (53 per cent) are clinically well with sputum negative for tubercle bacilli, and 4 (11 per cent) are still salvable. Seven (18 per cent) are hopelessly ill, and 7 (18 per cent) are dead.

TABLE 5

BILATERAL SURGICAL PROBLEMS—38 CASES

Rhode Island State Sanatorium—January, 1947, to January, 1952

BOTH SIDES COMPLETED (28 CASES)		ONLY ONE SIDE NECESSARY (2 CASES)	ONLY ONE SIDE POSSIBLE (8 CASES)	
Thoracoplasty-thoracoplasty	1		Death after one side	4
Thoracoplasty-lobectomy	2		Condition too poor	4
Extrapleural-extrapleural	11			
Thoracoplasty-extrapleural	10			
Extrapleural-lobectomy	2			
Lobectomy-lobectomy	1			
Cavernostomy-cavernostomy-thoracoplasty	1			

Follow-up, August, 1952

	NUMBER OF CASES	CLINICALLY WELL; SPUTUM NEGATIVE FOR TUBERCLE BACILLI	"POSITIVE" SPUTUM OR UNSTABLE LESION BY ROENTGENOGRAPHY	ACTIVE OR PROGRESSIVE DISEASE OR RESPIRATORY CRIPPLE	DEAD
Both sides completed	28	18 (64%)	4 (14%)	3 (11%)	3 (11%)
Only one side necessary	2	2	0	0	0
Only one side possible	8	0	0	4	4
Totals	38	20 (53%)	4 (11%)	7 (18%)	7 (18%)

TABLE 6

ALL SURGICAL PROBLEMS—289 CASES

RESULTS AS OF AUGUST, 1952

Rhode Island State Sanatorium—January, 1947, to January, 1952

Dead: 22 (7.5%)		
Tuberculous	10	
Nontuberculous	12	
Living: 267 (92.4%)		
Clinically well—sputum negative for tubercle bacilli	233	(87.3%)
"Positive" sputum or unstable lesion on roentgenography	19	(7.1%)
Active or progressive disease or respiratory cripple	12	(4.5%)
Inadequate follow-up	3	(1.1%)

RESULTS IN ALL SURGICAL CASES

The results for the entire series of 289 cases accepted for surgical treatment of parenchymal disease in the five-year period between January, 1947, and January, 1952, are presented in table 6.

Twenty-two patients (7.5 per cent) are dead. Ten died of tuberculous infection, and 12 of nontuberculous causes. Only one tuberculous death occurred in

the postoperative period. Seven of the 12 nontuberculous deaths occurred in the postoperative period.

Two hundred and sixty-seven patients (92.4 per cent) are living. Of this group, 233 (87 per cent) are clinically well with sputum negative for tubercle bacilli, and 19 (7 per cent) are clinically well but have either tubercle bacilli in the sputum or an unstable lesion on serial roentgenograms. It is believed that the majority of these 19 patients will eventually be salvaged and transferred to the "negative sputum" group. Twelve patients are hopelessly ill, on the basis of either extensive disease or respiratory reserve. Data available were inadequate to permit classification of 3 living patients.

It is believed that these final results represent the full measure of the success or failure of this or any other program of surgical treatment. They indicate what has been accomplished in the treatment of all patients presented as needing surgical treatment to get well. They represent what has been accomplished using all the surgical procedures available, either singly or in combination.

Discussion

The five-year period included in the present study has been one of rapidly changing concepts in the treatment of pulmonary tuberculosis. During this time, the use of antimicrobial drugs has been introduced and developed to the present status of prolonged intermittent therapy. This alone has revolutionized the treatment of tuberculosis. It has increased the safety of resectional procedures. As a result, the indications for resection have been extended. In addition, plombage thoracoplasty, both extraperiosteal and extrapleural, has tended to replace the conventional thoracoplasty for the standard thoracoplasty indications. In recent years, only those patients with giant cavities not suitable for resection have been treated at the Rhode Island State Sanatorium by staged thoracoplasty. In these instances, which are few in number, the stages have been performed from below upward, the cavity being mobilized at the time of the first stage by extrapleural dissection to convert the posterior cavity to a laterally positioned one. This places the cavity in a more ideal position for collapse when the uppermost ribs are resected. During the first two years of the present study, case selection was not as ideal as it has been during the last three years.

The original theme of this paper was that the final results in the treatment of all surgical cases represent the only statistics of significance. Certain concepts which the writers consider to be basic and fundamental are concerned with this approach to analyzing the end results of surgical treatment.

Surgical statistics will vary directly with the type of risk the medical and surgical staffs working as a team are willing to accept for surgery. At the Rhode Island State Sanatorium, an attempt was made to extend surgical help to every patient who had a reasonable chance to get well. Of the 289 patients in the present report, 38 had bilateral surgical problems. Ten of the 38 were more than fifty years of age and 2 were sixty. Of the entire 289 patients, 2 were less than ten years of age, 12 were between fifteen and twenty, 234 were between twenty and

fifty, and 39 were more than fifty years of age. Twenty-one were more than fifty-five, and 10 were more than sixty years old. The 2 oldest patients were sixty-six years of age.

A program which includes the aged, patients with bilateral cavities, and those with marginal respiratory function naturally will have poorer end results than programs which reject the potentially salvable cases from such poor risk groups and relegate them to the chronic wards of tuberculosis hospitals. Years ago the concept of "the good chronic" as a patient not suitable for surgical treatment was justified. Today, it should be used with caution. The surgeon and physician alike should not use this concept as an excuse to avoid the difficult and hazardous task of treating such patients.

The results of any given surgical procedure are not of significance unless the relative place this procedure plays in the total surgical program is analyzed. This is especially true of wedge and segmental resection. The limited extent of these resections is evidence in itself of the fact that they represent the treatment of a very select group of patients with less tuberculosis than is found in patients treated by any other surgical procedure.

The results with any given surgical procedure can be compared with another only when it is being applied to the same type of case. It is unreasonable to compare the results of segmental resection, for instance, with those of thoracoplasty because the type and extent of disease in the two groups vary so much. Any thoracoplasty series contains a high percentage of patients with disease too extensive to be treated by segmental resection.

The treatment of any particular case should be accomplished with the simplest and safest procedure that produces good, permanent results. There can be little doubt that thoracoplasty in the hands of the vast majority of surgeons, probably all surgeons, is a safer procedure than any resection, including segmental resection. In the type of case now being treated by segmental resection in many clinics, the present writers believe that a one-stage, nondeforming plombage thoracoplasty can be used with comparable "sputum conversion" rates, lower morbidity and mortality rates, and with a lasting cure surpassed by no other operative procedure. Upon the shoulders of those who advocate segmental resection for such cases rests the responsibility of showing that segmental resection produces results superior to those from thoracoplasty when the same indications are used for both procedures. This is one of the most important problems to be solved in the surgical treatment of tuberculosis.

In order to salvage the greatest number of patients, the surgeon must be willing and capable of using "all the tools in the bag." The surgeon who refuses to use extrapleural procedures or cavernostomy because they carry some risk or offend his surgical principles undoubtedly will deny surgery to many patients who can be treated by no other method. The wise and timely use of all the available surgical procedures, singly or in combination, is paramount if all salvable patients are to be offered a chance to get well. The end results of all procedures in such a surgical program constitute the only true measure of its success or failure.

BILATERAL RESECTION IN PULMONARY TUBERCULOSIS[1, 2]

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INTRODUCTION

Although there have been numerous reports of bilateral pulmonary resections for bronchiectasis since Eloesser's first case report (1) in 1933, only very recently has mention been made of such intervention for pulmonary tuberculosis (2, 3). As pulmonary tuberculosis, like bronchiectasis, tends to involve both lungs and is now widely being treated by pulmonary resection, it is inevitable that other reports of bilateral resection will reach the literature. No doubt there are many cases which have not been reported. The purpose of the present paper is to relate the experience with 17 cases. All operations, with one exception, were performed by, or under the supervision of, the writers.

Pulmonary resection was not generally accepted in the treatment of tuberculosis until long after its applicability in bronchiectasis had become well established. Even then it was recommended only when there were bronchial complications, lesions such as "destroyed lung," "tension cavity," "tuberculoma," or in cases in which collapse therapy had failed to arrest the disease. The danger of bronchopleural fistula and postoperative "spread" or exacerbation seemed so great that resection usually was considered only when there appeared to be little chance of controlling the disease in any other way. These complications are no longer great hazards as a result of the use of streptomycin and other antimicrobial drugs which have become available since 1947. Today, many thoracic surgeons and chest physicians recommend resections for lesions which formerly would have been considered suitable for treatment by bed rest, either alone or with the aid of collapse therapy. With the mortality of pulmonary resection and the incidence of complications reduced to low figures, physicians have been impressed by such things as the lack of chest deformity, even with a tailoring thoracoplasty, the elimination of the late complications of collapse procedures, and the material reduction in the period of convalescence.

There is fairly wide acceptance of the concept of Medlar and his colleagues (4) that certain tuberculous lesions, even though treated adequately according to standards which have been accepted in the past, remain as necrotic "encapsulated" foci from which spread or reactivation of disease may occur through bronchial communications. The belief that such foci should be removed has seemed to broaden greatly the indications for resection. Since such small areas of disease can be removed by segmental, subsegmental, and wedge techniques, an increasing number of bilateral resections will doubtless be performed. The present

[1] From the Division of Thoracic Surgery, University of Oregon Medical School, the University State Tuberculosis Hospital, Portland, Oregon; and Matson Memorial Hospital for Diseases of the Chest, Milwaukie, Oregon.

[2] Presented before the Medical Session, as part of the symposium on *Surgery in the Treatment of Tuberculosis*, at the 49th annual meeting of the National Tuberculosis Association, Los Angeles, California, May 19, 1953.

Case	Age	Sex	Stage	Previous Collapse Therapy	FIRST RESECTION				Ind
					Indication	Extent and Date	Associated Procedures	Complications	
1. L. Sp.	21	F	Far advanced, 1948	Right pneumothorax, 1948; left pneumothorax, 1949–1950	Pneumothorax failure (atelectasis and open cavity)	Right upper lobe, September 1948	Decortication; 5-rib thoracoplasty 3 weeks later	Late empyema with bronchopleural fistula	Pneumot (open ca lobe)
2. L. P.	37	F	Minimal, 1951	None	"Tuberculoma"	Wedge from apical segment of left upper lobe October 1951	None	Paralysis of left diaphragm	"Tuberc
3. R. H. (figure 1)	31	M	Far advanced, 1940	Right pneumothorax, 1940–1945; left pneumothorax, 1944–1947; left phrenemphraxis, 1945	Incidental to decortication	Right upper lobe, July 1951	Decortication and 4-rib thoracoplasty	None	Pneumot (open ca lung re-e
4. L. A.	45	M	Far advanced, 1932	Right permanent phrenic paralysis, 1935; right extrapleural pack, 1940; right thoracoplasty, 1940; right 3-stage rev. thoracoplasty, 1941; left pneumothorax, 1950; pneumoperitoneum, 1950–1951	Thoracoplasty failure	Right upper lobe, 1948	None	None	Pneumot (tension
5. M. P. (figure 2)	27	F	Far advanced, 1951	None	"Destroyed lobe"	Left upper lobe, May 1951	4-rib thoracoplasty	None	Tubercul chial dis tive" spu
6. M. A. (figure 3)	36	F	Far advanced, 1951	Right 2-stage, 7-rib thoracoplasty, 1951	Thoracoplasty failure	Right upper lobe and superior segment of right lower lobe, February 1951	None	None	Large res focus
7. P. L.	16	F	Far advanced, 1944	Left pneumothorax, 1945; right pneumothorax, 1952	Pneumothorax failure (atelectasis and open cavity)	Left upper lobe, August 1945	None	Late reactivation	Elective cavity)
8. L. St. (figure 4)	38	F	Far advanced, 1947	Left pneumothorax, 1947–1952; right phrenemphraxis, 1947; pneumoperitoneum, 1947–1952	Incidental to decortication	Subsegment of the posterior basal segment and superior segment of left lower lobe, January 1952	Decortication	Postoperative psychosis	Large c "positive
9. W. D.	34	M	Far advanced, 1945	Right 2-stage, 7-rib thoracoplasty, 1946; left pneumothorax, 1948–1952	Incidental to decortication	Wedge from apical posterior segment of left upper lobe, June 1952	Decortication	None	Thoracop
10. B. C. (figure 5)	38	F	Minimal, 1946	None	Probable tuberculous bronchial disease (hemoptysis, "positive" sputum cultures)	Apical segment of right upper lobe, October 1951	None	None	Probable bronchial moptysis cultures)
11. K. G. (figure 6)	29	F	Moderately advanced, 1952	None	Elective (upper lobe cavity)	Apical posterior and anterior segments of left upper lobe, July 1952	None	None	Elective cavity)
12. I. C. S. (figure 7)	26	F	Far advanced, 1944	Left pneumothorax, 1946–1951	Probable tuberculous bronchial disease	Apical posterior segment of left upper lobe and superior segment of left lower lobe, February 1952	Decortication	None	Probable bronchial
13. C. A.	25	F	Far advanced, 1947	Left pneumothorax, 1947–1952	Pneumothorax failure	Apical posterior and anterior segments of left upper lobe and superior segment of left lower lobe, August 1952	Decortication and 4-rib thoracoplasty	None	Probable bronchial ("positiv
14. E. L.	38	F	Far advanced, 1949	Right pneumothorax, 1949–1950; left pneumothorax, 1949–1951	Pneumothorax failure	Superior segment of right lower lobe and wedge from anterior segment of right upper lobe, March 1950	None	None	"Tuberc
15. M. B. (figure 8)	21	F	Minimal, 1952	None	"Tuberculoma"	Wedge from apical segment of left upper lobe, December 1952	None	None	"Tuberc
16. M. B. F.	18	F	Minimal, 1944	None	Tuberculous bronchial disease ("positive" sputum)	Right lower lobe, October 1945	None	None	Tubercul chial dis tive" spu
17. D. S.	35	F	Far advanced, 1949	Right pneumothorax, 1950–1951; left pneumothorax, 1952	Caseous focus under pneumothorax	Apical and posterior segments of right upper lobe, July 1951	Decortication	None	Elective cavity)

TABLE 1
Case Summaries

SECOND RESECTION				Recent Status	Remarks
Indication	Extent and Date	Associated Procedures	Complications		
neumothorax failure pen cavity in lower be)	Superior segment of left lower lobe, August 1950	None	Empyema and bronchopleural fistula	Dead	
Tuberculoma"	Wedge from apical segment of right upper lobe, January 1952	None	None	Arrested (14 months) V	
neumothorax failure pen cavities when ng re-expanded)	Apical posterior segment of left upper lobe, January 1952	Decortication	None	Arrested (14 months) IV	
neumothorax failure ension cavity)	Apical subsegment of apical-posterior segment of left upper lobe, February 1952	None	Early exacerbation of disease on opposite side	Arrested (4 months) IV	
uberculous bronchial disease ("positive" sputum)	Apical and posterior segments of right upper lobe, February 1952	None	Clotted exudate	Inactive (14 months) V	Contralateral bronchopneumonia
rge residual caseous us	Superior segment of left lower lobe and lingula, March 1952	None	None	Arrested (12 months) IV	
ctive (upper lobe rity)	Apical and posterior segments of right upper lobe, March 1952	None	None	Arrested (12 months) IV	Delivered full-term infant, May 1953
rge caseous foci; sitive" sputum	Anterior, lateral, medial, basal segments of right lower lobe, anterior segment of right upper lobe; enucleation of tuberculoma from superior segment of right lower lobe, April 1952	Decortication	None	Arrested (12 months) IV	
oroplasty failure	Apical segment and adjacent subsegments of anterior and posterior segments of right upper lobe, August 1952	None	None	Arrested (9 months) IV	
obable tuberculous onchial disease (hemoptysis; "positive" tures)	Apical posterior segment of left upper lobe and wedge from lingula, September 1952	None	None	Inactive (6 months) V	
ctive (upper lobe rity)	Posterior segment of right upper lobe, November 1952	None	None	Arrested (5 months) II	First operation during second trimester of pregnancy
obable tuberculous onchial disease	Right upper lobe, lateral segment of right middle lobe, superior segment of right lower lobe, wedge from basal segment of right lower lobe, December 1952	None	None	Arrested (4 months) II	
obable tuberculous onchial disease positive" sputum)	Right upper lobe, January 1953	None	None	Arrested (3 months) II	
uberculoma"	Lingula of left upper lobe, February 1953	None	Diabetic acidosis	Undetermined; no evidence of active disease	Diabetes mellitus moderately severe
uberculoma"	Wedge from posterior segment of right upper lobe, February 1953	None	None	Undetermined; no evidence of active disease	Both resections during the second trimester of pregnancy
bercuious bronchial disease ("positive" sputum)	Superior segment of left lower lobe, October 1949	None	None	Inactive (43 months) V	
ctive (upper lobe rity)	Apical posterior segment of left upper lobe, October 1952	None	Residual air pocket in apex, non-infected	Arrested (6 months) III	

writers are aware that the advisability of resecting such localized caseous lesions can be contested on bacteriologic and pathologic grounds and that the response to the new drugs may eventually change the present concepts. Only the accumu-

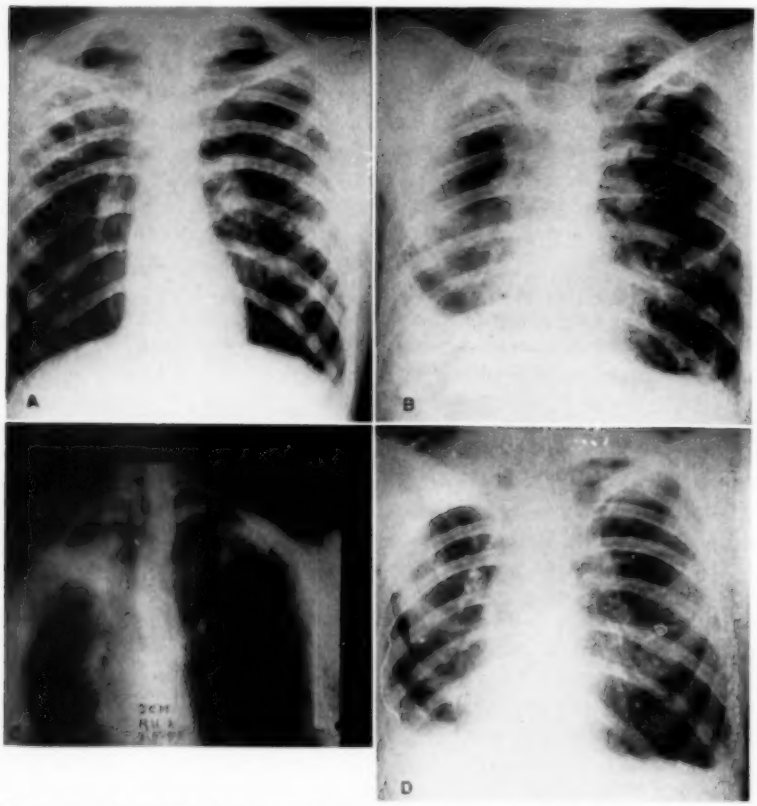

FIG. 1. Case 3 (R. H.). *A*. Original roentgenogram. *B*. Admission roentgenogram. Previous therapy included bilateral pneumothorax, left phrenemphraxis, a total of four periods of hospitalization. *C*. Admission tomogram showing left apical cavity. *D*. Twenty months after right decortication, resection of right upper lobe, and thoracoplasty; fourteen months after resection of apical-posterior segment of the left upper lobe and decortication.

Clinical status: Pulmonary tuberculosis arrested (14 months), improved exercise tolerance.

lation of data for a period of years will finally settle the puzzling questions of how much to resect and when.

OBSERVATIONS

Clinical Material

Three males and 14 females, all white, with ages ranging from sixteen to forty-five, were operated upon. The interval between the original diagnosis of pulmonary tuberculosis and

the first resection varied from one month to sixteen years and averaged four years. The tuberculosis was classified as minimal in 4, moderately advanced in one, and far advanced in 12 patients. The sputum was positive for acid-fast bacilli before the first operation in all but one patient, and 14 had sputum positive for tubercle bacilli between the first and second resections. In most patients, however, under antimicrobial therapy, there was a marked reduction in numbers of bacilli, or actual "sputum conversion," before surgery.

In the presentation of the cases (table 1, figures 1–8), data concerning antimicrobial and other medical therapy are omitted. Several patients received repeated and prolonged courses of streptomycin or dihydrostreptomycin. Para-aminosalicylic acid (PAS) was used in conjunction with streptomycin when it became available; and, more recently, isoniazid has been used with streptomycin or with PAS and streptomycin in some cases. As a general rule, streptomycin is now given twice weekly, although it has usually been given daily for a week or two immediately following surgery. The drugs have been discontinued six to

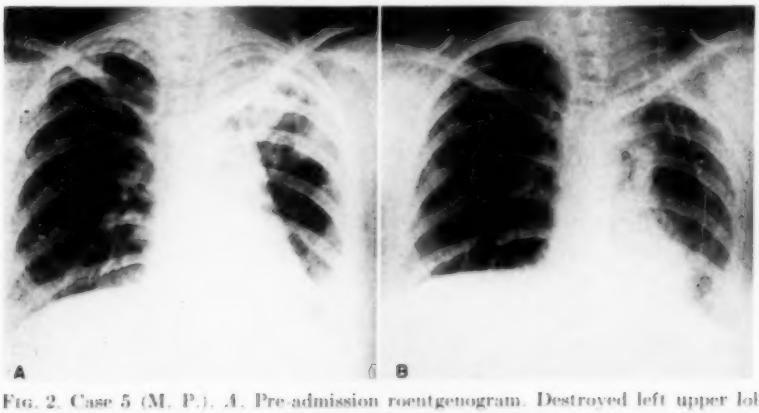

FIG. 2. Case 5 (M. P.). *A*. Pre-admission roentgenogram. Destroyed left upper lobe; minimal infiltrations in right apex. *B*. Twenty months after left upper lobectomy and thoracoplasty; eleven months after resection of apical and posterior segments of the right upper lobe for suspected tuberculous bronchial disease with sputum positive for tubercle bacilli. The second resection was complicated by organized exudate on the operated side treated by enzymatic debridement and postoperative contralateral bronchopneumonia.
Clinical status: Pulmonary tuberculosis inactive (14 months).

twelve weeks after surgery in patients showing no residual parenchymal disease either grossly at the time of the operation or by roentgenogram during the postoperative period.

In general, pulmonary function pre- and postoperatively received clinical evaluation only. Circumstances did not permit systematic bronchospirometric procedures in this series, and the data obtained on some of the cases are omitted as being noncontributory. The patient's ability to tolerate pulmonary resection, from the standpoint of respiratory reserve, was estimated on the basis of physical and roentgenographic findings and on his tolerance of exercise as determined by history and observation. When fibrotic pleural changes were present, the possibility of regaining function by decortication of the conserved portions of the lungs was taken into consideration. Six patients had constrictive pleural "peels" as a result of artificial pneumothorax with clinical evidence of mild to marked functional impairment. In one of these 6, both lungs were so involved. Another had had tuberculous empyema, unassociated with pneumothorax, five years prior to his first resection. Three patients had had previous thoracoplasties, all considered failures, although one had been observed for only seven months prior to resection.

One patient had moderately severe diabetes mellitus; one had mild to moderately severe

bronchial asthma. One patient was pregnant at the time of the first operation, while another had both operations during a single pregnancy. Both pregnancies were carried to term uneventfully, and another patient has completed a normal pregnancy since her second operation.

It is believed that, without excisional surgery on at least one side, the prognosis of these patients for eventual attainment of a clinical status of inactive tuberculosis was definitely poor in 11 and only fair in 6.

Indications

The indications for the first and second resection in each patient in the series are listed in table 2. It is difficult to place indications for resection in tuberculosis in specific pigeonholes, since there may be more than one indication and since

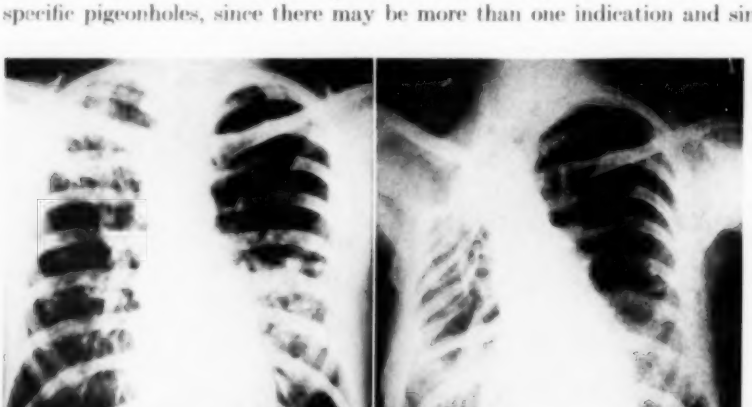

FIG. 3. Case 6 (M. A.). *A*. Admission roentgenogram. Thoracoplasty failed to control disease on the right. *B*. Twenty-six months after resection of right upper lobe and superior segment of the right lower lobe; twelve months after resection of the superior segment of the left lower lobe and lingula for large residual caseous foci.

Clinical status: Pulmonary tuberculosis arrested (12 months).

experts disagree on what constitutes an "elective" resection. The present writers have favored the trend away from collapse therapy and in the direction of excisional surgery in the treatment of tuberculous patients. Pneumothorax therapy has virtually been abandoned in the writers' practice, and approximately 20 resections are performed for every primary thoracoplasty or extrapleural operation.

Pneumothorax failure: Pneumothorax failure was the indication for 7 resections. Thoracoplasty or extrapleural pneumothorax was considered unsuitable because of the development of "atelectasis" in the cavity-containing lobe in 2 cases and because of a "tension"-type cavity in one. In 2 patients, the location of cavities in the lower lobes made resection more advisable than further attempts at collapse. In the remaining 2 cases, resection was chosen rather than thoraco-

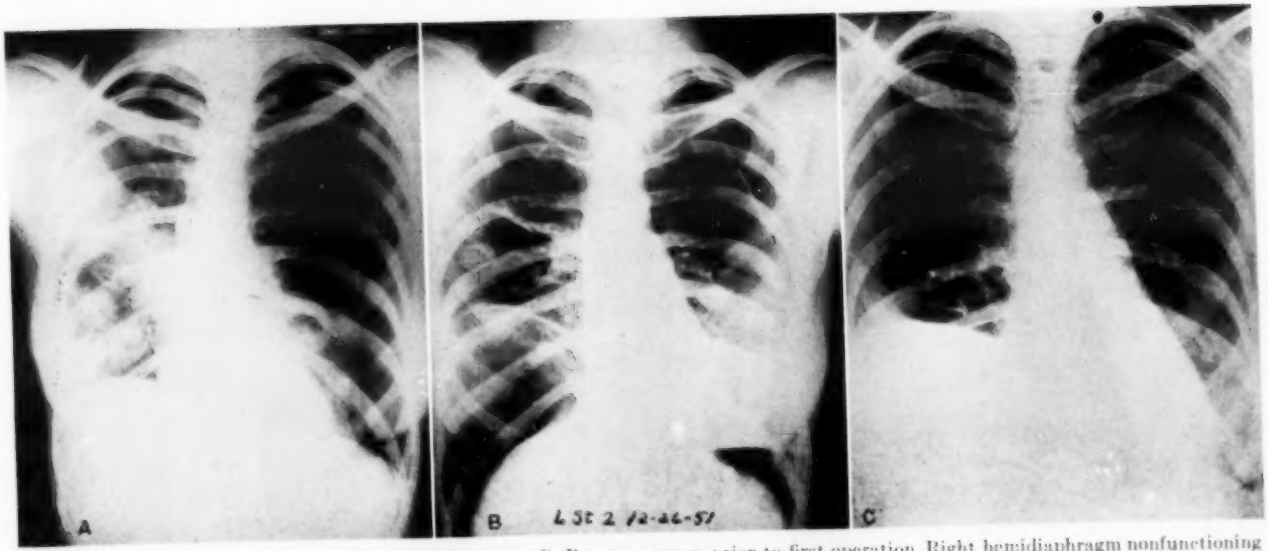

FIG. 4. Case 8 (L. St.). *A*. Admission roentgenogram. *B*. Roentgenogram prior to first operation. Right hemidiaphragm nonfunctioning following phrenemphraxis and pneumoperitoneum therapy; thick "peel" over left lung. The sputum was positive for tubercle bacilli. *C*. Fifteen months after left decortication and resection of the superior segment and a posterior basal subsegment of the left lower lobe; twelve months after resection of the anterior, medial, and lateral basal segments of the right lower lobe, enucleation of a "tuberculoma" in the superior segment of the lower lobe, and decortication of an existing pleural "peel".

Clinical status: Pulmonary tuberculosis arrested (12 months); improvement in exercise tolerance.

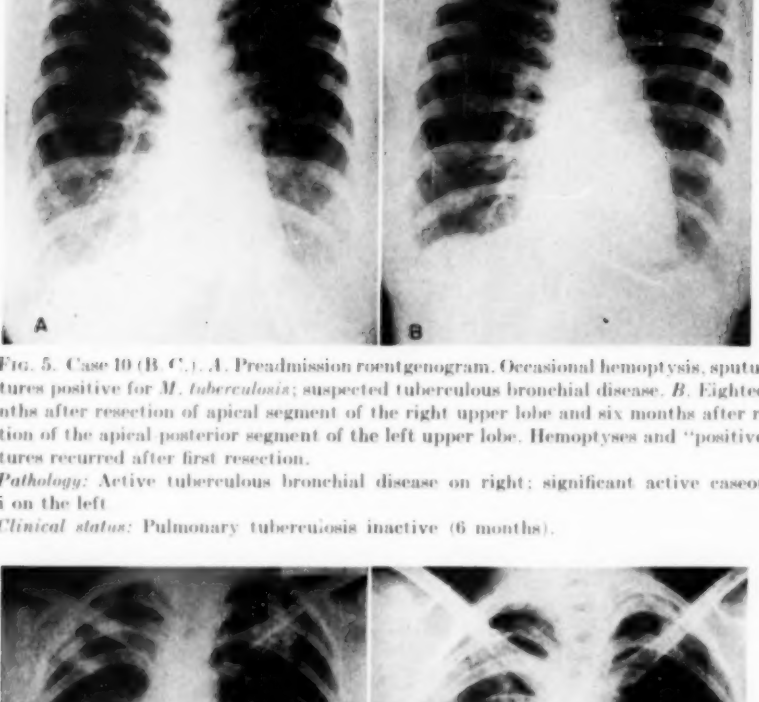

FIG. 5. Case 10 (B. C.). *A*. Preadmission roentgenogram. Occasional hemoptysis, sputum cultures positive for *M. tuberculosis*; suspected tuberculous bronchial disease. *B*. Eighteen months after resection of apical segment of the right upper lobe and six months after resection of the apical-posterior segment of the left upper lobe. Hemoptyses and "positive" cultures recurred after first resection.

Pathology: Active tuberculous bronchial disease on right; significant active caseous foci on the left.

Clinical status: Pulmonary tuberculosis inactive (6 months).

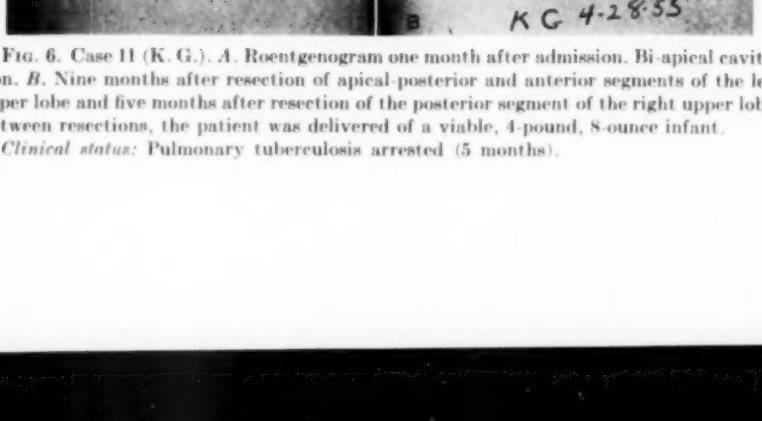

FIG. 6. Case 11 (K. G.). *A*. Roentgenogram one month after admission. Bi-apical cavitation. *B*. Nine months after resection of apical-posterior and anterior segments of the left upper lobe and five months after resection of the posterior segment of the right upper lobe. Between resections, the patient was delivered of a viable, 4-pound, 8-ounce infant.

Clinical status: Pulmonary tuberculosis arrested (5 months).

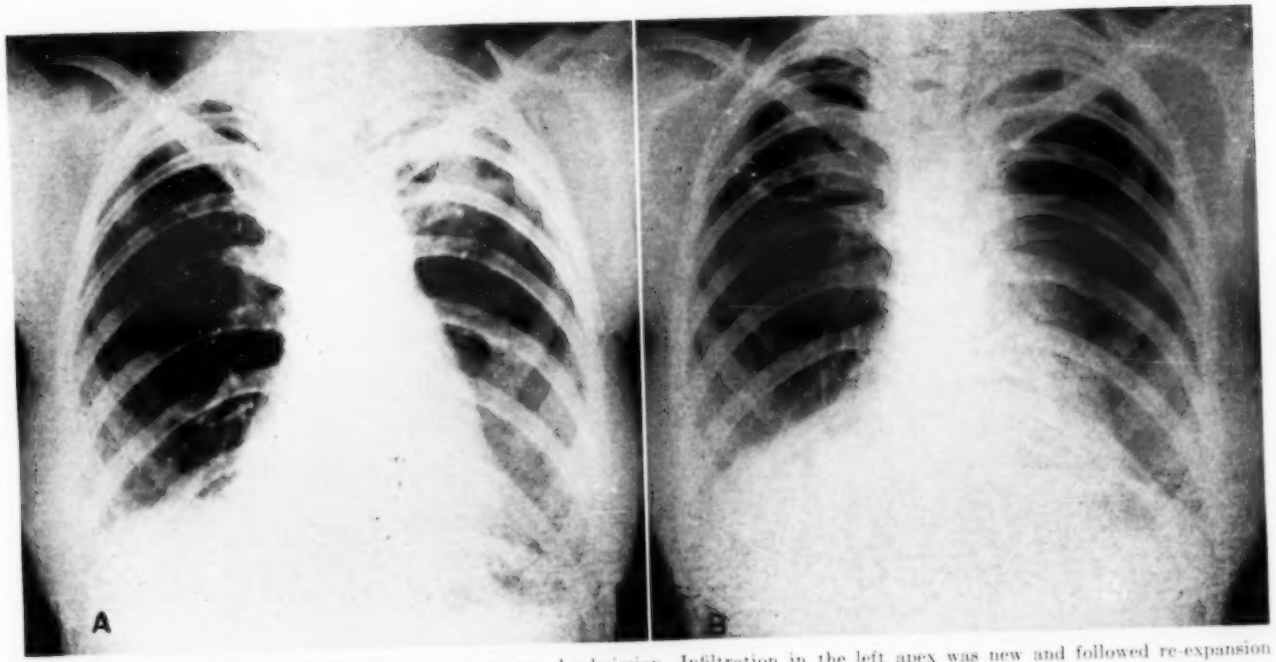

FIG. 7. Case 12 (I. C. S.). *A*. Roentgenogram at second admission. Infiltration in the left apex was new and followed re-expansion of pneumothorax. Previous therapy: left pneumothorax five years for cavitary disease; cavity in superior segment of right lower lobe had apparently closed on medical management. Three previous admissions to other hospitals since 1944. *B*. Fourteen months after resection of apical-posterior segment of the left upper lobe, superior segment of the lower lobe, and decortication; four months after resection of the right upper lobe, lateral segment of the right middle lobe, superior segment of the right lower lobe, and wedge resection from a basal segment.

Clinical status: Pulmonary tuberculosis arrested (4 months).

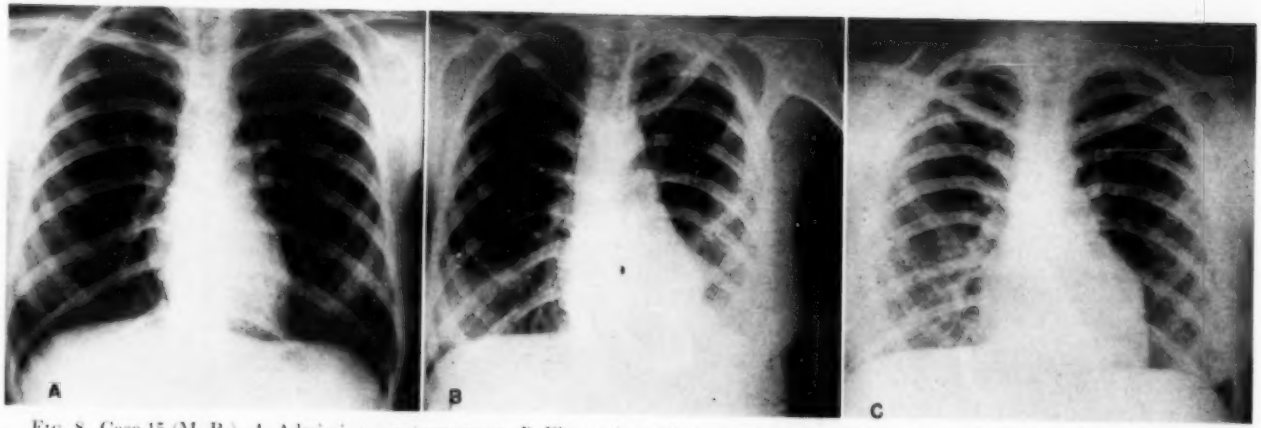

FIG. 8. Case 15 (M. B.). *A*. Admission roentgenogram. *B*. Eleven days after resection of a "tuberculoma" from the left apex. The round lesion in relation to the second right rib anterolaterally was enlarging. *C*. Two months after wedge resection of the "tuberculoma" on the right. Both operations were performed through short submammary incisions during the second trimester of pregnancy.

Clinical status: Undetermined; no present evidence of active tuberculous disease.

plasty because of the desirability of a concomitant decortication in order to improve function. In one of these, it seemed mandatory that function be improved before significant chronic disease in the contralateral lung could be attacked. Subsequent examinations of the specimens in both cases reveal that further collapse therapy could hardly have been expected to arrest disease because of the thickness of the pleural "peels" and cavity walls. Resection appeared to offer the only hope of disease arrest in this group.

Thoracoplasty failure: Thoracoplasty failure constituted the indication for 3 of the operations. One patient, whose first resection was performed elsewhere, had had a revision thoracoplasty and continued to have sputum positive for tubercle bacilli prior to that resection. One had a 2 cm. cavity under a thoracoplasty performed six years earlier. One patient, having a 5 cm. upper lobe cavity originally, continued to have many tubercle bacilli in the sputum seven months after thoracoplasty, despite good medical therapy. Resection was the only satisfactory method of treatment in these 3 cases.

TABLE 2

INDICATIONS FOR BILATERAL RESECTION IN PULMONARY TUBERCULOSIS

Pneumothorax failure	7
Thoracoplasty failure	3
Destroyed lobe	1
Tuberculous bronchial disease	8
Localized caseous foci	8
Incidental to decortication	3
Upper lobe cavitation ("elective")	4
Total	34

Destroyed lobe: A destroyed lobe previously untreated by collapse measures was the indication for one operation. Thoracoplasty might have controlled the disease, but resection was thought to offer a much better prognosis.

Localized caseous foci: Localized caseous tuberculous foci of the type described by Ryan, Medlar, and Welles (4), often loosely designated "tuberculomas," were the indication for 8 resections. In one patient large, well-circumscribed, partially calcified, bi-apical "tuberculomas" might have remained stable without surgery. Another patient, following the removal of a 1.5 cm. "tuberculoma" on one side and while still at bed rest and taking antimicrobial drugs, developed enlargement of a contralateral circumscribed round lesion. It was believed that her prognosis was only fair without the second resection. The remaining 4 patients previously had had extensive infiltrations which on medical therapy resorbed and contracted, leaving large, discrete foci. Two of these patients had occasionally discharged tubercle bacilli in their sputum. The other had "negative" sputum following a previous contralateral resection, but the remaining lesion was of such size as to be considered unstable, which, in fact, was borne out by the subsequent pathologic examination.

Tuberculous bronchial disease: Tuberculous bronchial disease, actual or sus-

pected, was the primary indication for 8 resections. In 6 instances, residual, stringy, and small stellate or nodular upper lung densities were present following long-treated exudative disease. All showed roentgenographic evidence of instability as well as sputum positive for tubercle bacilli. Cavitation had not at any time been demonstrated clinically in 4 of the 6 patients, and none had cavities at the time of resection. One patient who had bilateral disease of this nature had previously had cavities, both of which had closed, one under the influence of pneumothorax therapy. Concomitant decortication was a secondary indication for thoracotomy in this patient, and it subsequently made possible the contralateral resection by substantially improving pulmonary function.

One patient had extensive bronchiectasis, with some associated parenchymal infiltration, in the right lower lobe. Her sputum, positive for tubercle bacilli before this lobe was removed in 1945, remained positive until 1949, and the superior segment of the left lower lobe was resected. Bronchographically demonstrated bronchiectasis in the latter segment was the only evident pathology prior to the second resection and, since the patient was essentially asymptomatic, "positive" sputum was the only indication for its resection. She has been clinically well with sputum negative for *M. tuberculosis* during the ensuing three and one-half years.

Resection incidental to pulmonary decortication: Resection incidental to pulmonary decortication following pneumothorax therapy was done in 3 instances. Decortication was done chiefly in the hope of improving function sufficiently to permit contralateral resection. Cavities, present before pneumothorax in 2 of these, had closed satisfactorily, and in all of the patients the disease had seemed to be clinically stable. At surgery, however, the decorticated lung was found to have lesions which were potentially unstable. These were resected, and the pathologic findings confirmed the need for resection.

Upper lobe cavities: Upper lobe cavitation was the indication for 4 resections, and these can be listed as "elective," since none of the patients had been treated by previous collapse therapy.

Extent of Resections

The total amount of lung tissue removed per case (both resections) varied from less than one pulmonary segment (in each of 2 patients having bilateral wedge resections) to approximately 7 segments. At first there were more complete lobectomies than segmental or other more limited resections, but in the middle of the series, as the feasibility and safety of segmental and wedge techniques became better established, the ratio was reversed.

In this series of 17 cases, 9 complete lobes, 32 segments, and 8 subsegments or wedges were removed. An average total of 4 segments, roughly the equivalent of a left upper or lower lobe, was removed in each patient at the two operations. Assuming, from observation at surgery, that the 18 segments of the two lungs as described by Jackson and Huber (5) have roughly equivalent volumes, the percentage of total lung volume removed varied from 3 to 40 per cent, with an average of 22 per cent. On this basis, in none of these cases has there been removed

a volume of lung as large as the equivalent of the entire left lung (8 segments, or 45 per cent).

In figure 9 is shown diagrammatically the extent of resection and of residual, apparently inactive foci in the cases reported here. Associated surgical procedures are also indicated.

Results

In table 3 is recorded the clinical status of the 17 patients with completed bilateral resections according to the National Tuberculosis Association standards. All but one of the 10 patients with disease classified as "arrested" have shown no roentgenographic or other evidence of active disease since their second operations, but their disease fails technically to meet the NTA requirement for "inactive" status because an insufficient number of sputum or gastric cultures have been performed. The exception (Case 4) showed evidence of an infiltration in an

TABLE 3

RECENT CLINICAL STATUS OF 17 PATIENTS WHO WERE SUBJECTED TO BILATERAL RESECTION ACCORDING TO NATIONAL TUBERCULOSIS ASSOCIATION STANDARDS

Inactive (6–43 months)	3
Arrested (3–14 months)	11
Unclassified	2
Dead	1
Total	17

adjacent segment after segmental resection, and the patient's sputum was occasionally positive for tubercle bacilli on concentration, but now, thirteen months after his second resection, he is classified "arrested (4 months)." Two patients whose surgical procedure was completed within the past three months have not been classified. None has evidence of active pulmonary or bronchial tuberculosis. The fatality was due to bilateral mixed empyema with bronchopleural fistulas. This patient was given prolonged courses of streptomycin, often without PAS, which she did not tolerate well. Streptomycin-resistance studies were not performed, but it was believed that, at least in the latter part of her illness, she was afforded no benefit by the drug. It was also believed that the bronchopleural fistula on the right could have been managed satisfactorily during the first admission had she not left against medical advice soon after operation. Right thoracotomy to close the fistula might have prevented the right empyema and subsequent exacerbation on the left, which led to her death. This death, however, was attributable to the surgery.

Although it did not always seem possible or advisable to remove all palpable foci of disease, those which were left were thought to be relatively unimportant. This belief appears to be borne out by the occurrence of a new infiltration in only 2 patients; one was a minor one which soon resolved; one was arrested by subsequent thoracoplasty.

Although several patients have clinical evidence of a moderate degree of pul-

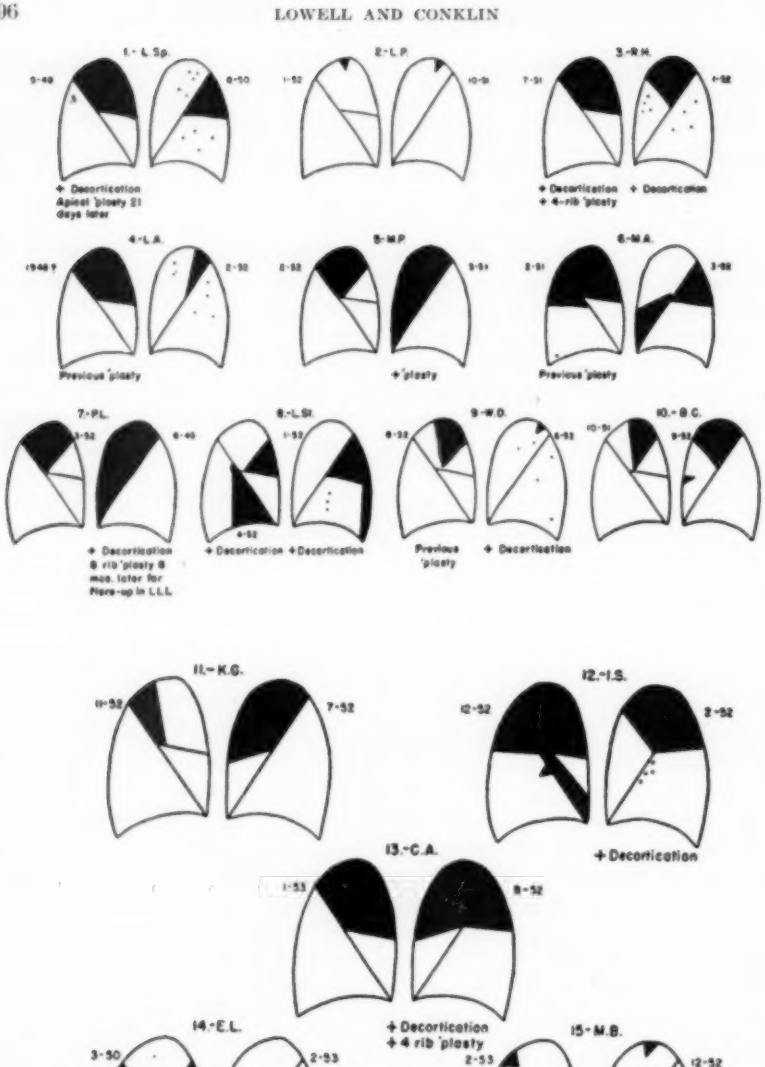

FIG. 9. A diagrammatic representation of 15 bilateral resections. The black areas represent the portions of lung resected. Dots indicate apparently inactive foci not disturbed at the time of resection. Previous thoracoplasties, concomitant operations, and later thoracoplasties are noted.

monary functional loss, none except the patient who died has been a respiratory cripple, and at least one has more reserve than before the first resection as a result of concomitant decortications. Patient 7, who had six segments removed together with an extensive left thoracoplasty, has recently delivered a full-term infant without incident.

In all cases there was evidence of active tuberculous disease on pathologic examination of the operative specimens. This evidence consisted of one or more of the following: caseous foci having little or no encapsulation, satellite tubercles around caseous foci, bronchial tuberculous ulcerations, or cavitation. Cultures and acid-fast stains of the resected specimens were not made routinely.

The complications may be summarized as follows:

Bronchopleural fistula with empyema	2 (both in same patient, who died)
Bronchopleural fistula (persistent lung leak) without empyema	1
Postoperative exacerbation, same side	2
Phrenic paralysis (permanent)	1
Organized exudate, treated successfully with enzymatic debridement	1
Contralateral pneumonia	1

DISCUSSION

It is obvious that no final conclusions can be drawn from the few patients of the present series, many of whom have had their second resections within the past year. It seems to be the consensus, however, that most of the complications from pulmonary resection occur early, that is, within the first two months, and that early good results tend to be maintained with the passage of time. From this limited experience with bilateral resections, it is concluded that postoperative complications are no more frequent percentagewise than after unilateral resection. It is fortunate that the incidence of postoperative exacerbation has been low in the present series (2 instances), considering that it was sometimes necessary to leave palpable tuberculous foci.

Kergin (6) and others have shown that, with proper selection of cases, extensive bilateral resections can be performed for bronchiectasis without causing respiratory crippling. A number of patients have had both lower lobes, the middle lobe, and the lingula of the left upper lobe, a total of thirteen lung segments, removed without excessive impairment of respiratory function, and it is not uncommon to remove eleven segments of lung (both lower lobes and lingula). The present writers question the advisability of removing an equally large number of upper lung segments. It seems unlikely that any patient could exist comfortably with only the basal segments of the lower lobes, a total of seven segments, remaining.

It is considered advisable to obliterate by thoracoplasty any sizable dead space remaining after normal inflation of nonresected portions of the lung by the anesthetist (7). Thus, it is hoped to conserve function by preventing overdistention and diaphragmatic limitation. Such a tailoring thoracoplasty may also

decrease the incidence of postoperative "spreads" or reactivation of nonresected lesions. Its value in the prevention or control of postoperative bronchopleural fistula and empyema is beyond question. Except in limited resections, where the remaining lung tissue largely fills the pleural cavity, or in lower lung resections, where the diaphragm rises easily to obliterate the space, it is believed that a thoracoplasty should be performed at the time of the resection.

To date the writers have not performed a resection-thoracoplasty following a contralateral resection-thoracoplasty. A decortication-thoracoplasty has been performed successfully, however, in a patient who had a previous contralateral decortication and resection-thoracoplasty. The successful outcome of this and similar cases suggests that certain patients could tolerate bilateral resection-thorocoplasty, with removal of as much as both upper lobes and possibly even the right middle lobe or superior segments of both lower lobes. This would be a total of nine segments, or two more than the maximum number removed in any case in this series. It should be pointed out, however, that one is limited in performing a second combined operation by the temporary paradoxical motion of the chest wall and concomitant reduction in respiratory reserve, which might result in uncontrollable respiratory failure during the early postoperative period.

In order to avoid paradoxical movement of the chest wall, employment of some modification of the conventional thoracoplasty, such as the Overholt costoversion thoracoplasty, or extraperiosteal plombage with or without thoracoplasty, may be considered. These seldom seem applicable, however, for during the resection it is often desirable or necessary to remove parietal pleura, particularly over adherent diseased lung tissue or when decortication is performed. The method of Trapp (8), endorsed by Coddington (9), which employs plaster splints to stabilize the chest wall following thoracoplasty, could probably be used to advantage. An obvious alternative is to perform some type of thoracoplasty several weeks in advance of a planned necessary resection when it appears that paradoxical motion might present a significant problem were resection and thoracoplasty to be performed at the same time.

In the 17 patients reported here, concomitant thoracoplasty was performed three times. In 2 cases a thoracoplasty was performed some time following resection, and it is believed that concomitant thoracoplasty might have prevented, in these patients, the complications and the one death which occurred. Three others had had previous thoracoplasties, not planned as a preliminary to resection, although in one the need for a subsequent resection was considered likely.

In most of the cases the decision to perform pulmonary resection was based upon generally accepted indications. However, 4 resections of upper lobe segments containing cavities which might have been closed by pneumothorax or thoracoplasty were performed. During the past few years the writers have preferred resection, whenever applicable, believing that it provides greater prospect of permanent arrest of the disease in a shorter period of time, with less loss of function and fewer long-term complications. The employment of the term "elective" in connection with such operations is, in a sense, a misnomer.

Application of bilateral resection in tuberculosis differs from that in bronchiec-

tasis. In pulmonary tuberculosis, the need for bilateral resection frequently does not become apparent until after the first resection has been performed. A contralateral collapse procedure, such as some type of extrapleural pneumonolysis, may often seem less hazardous and more conserving of function than resection. As indicated above, when significant post-pneumothorax or post-effusion "peel" hampers pulmonary function, the decortication and resection have been performed first (whether the latter is considered definitely indicated or "incidental") before resecting what seem to be more significant lesions in the contralateral lung. Otherwise, since the primary purpose of resection is to eradicate tissue which is the source of infectious sputum, the more involved side is operated upon first. In 12 of the patients, indications for the second operation were not established until some time following convalescence from the first, although the possibility was definitely recognized in 4 patients. Before and between operations, every effort is made to obtain nearly maximum improvement of all lesions by medical management, sometimes including collapse therapy, particularly pneumoperitoneum.

When bilateral resection was planned before the first resection, an average of three and one-half months elapsed between operations. It is believed that only approximately three months are usually required to stabilize function in the operated lung sufficiently to permit the second operation, although from bronchospirometric data it has been observed that function of a decorticated lung may show continuing improvement for a period of eighteen months or longer. Clinical evaluation, without resort to function studies, usually suffices to determine when and if a given patient is ready for, and can tolerate, the second operation. Other surgeons, to whom routine bronchospirometric studies are readily available, may think differently about this point. When bilateral resections are required, it is advisable, naturally, to keep the interval between the two operations at a minimum in order to shorten morbidity and for economic reasons. The discharge of some of the patients two or three months following resection was often forced by economic considerations or by the shortage of beds for tuberculous patients in this area. A minimum of six months' hospitalization following the second resection would ordinarily be recommended.

The writers cannot presume to discuss with authority the future place of bilateral resection for tuberculosis on the basis of the present small experience. So many of the decisions involved, e.g., which patients to select, how much to resect and when, how often to do concomitant thoracoplasty, when to decorticate, are based upon empirical factors rather than on the well-established facts of physiology and pathology or upon the wide experience which comes with the use of some procedure, like thoracoplasty, through the years. The writers hope that the questions proposed and the ideas discussed in the present paper will induce others to contribute their experiences with this relatively new development in the surgical treatment of tuberculosis.

Another question which merits discussion is that of choosing "good risks" or "poor risks" for bilateral surgery. Most of the patients were in satisfactory clinical condition except for variable limitation in pulmonary function. Even so, the

majority of them were considered, on the basis of past experience, to have a poor prognosis for eventual arrest of their disease without resection on one or both sides.

It is believed that wider application of bilateral pulmonary resection in pulmonary tuberculosis may go far toward reducing morbidity, shortening convalescence, and reducing waiting lists for beds in tuberculosis hospitals. It is also believed that it may offer the only chance for cure and rehabilitation to large numbers of persons who have heretofore been designated as "good chronics" or incurables.

SUMMARY

Seventeen patients with pulmonary tuberculosis were treated by bilateral pulmonary resection.

One patient died from progressive disease and complications. Two patients were operated upon too recently for classification, but have no evidence of active parenchymal tuberculosis. Three patients have lesions designated as "inactive" at six to forty-three months, and in 11 patients the disease is classified as "arrested" three to fourteen months after the bilateral procedure. At least 10 of these patients would have been considered to have had incurable disease without one or both resections.

Bilateral resections in pulmonary tuberculosis have become more widely applicable as a result of antimicrobial therapy, which decreases the incidence of complications, and improved surgical techniques which permit resection of sublobar portions of the lung.

It is anticipated that bilateral resection will shorten morbidity and provide the only means of cure for large numbers of patients with pulmonary tuberculosis.

SUMARIO

La Resección Bilateral en la Tuberculosis Pulmonar

Diecisiete tuberculosos pulmonares fueron tratados con la resección pulmonar bilateral.

Un enfermo murió de tuberculosis evolutiva y complicaciones. Dos sujetos han sido operados hace demasiado poco tiempo para poder classificarlos, pero no muestran signos de tuberculosis parenquimatosa activa. Tres enfermos están "inactivos" (de seis a cuarenta y tres meses) y 11 están "estacionados" (de tres a catorce meses). A lo menos 10 de esos sujetos hubieran sido considerados incurables, de no haber sido por una o ambas resecciones.

Las resecciones bilaterales en la tuberculosis pulmonar han encontrado aplicación más amplia a consecuencia de las medicaciones antimicrobianas, que disminuyen la incidencia de complicaciones, y de las perfeccionadas técnicas quirúrgicas, que permiten la resección de porciones sublobulares del pulmón.

Confíase en que la resección bilateral acortará la morbidad y facilitará el único medio de curación a un gran número de enfermos de tuberculosis pulmonar.

RESUME

Résection bilatérale dans la tuberculose pulmonaire

Dix-sept malades atteints de tuberculose pulmonaire ont été traités par résection pulmonaire bilatérale.

La mort d'un des malades est attribuée à l'évolution de la maladie et à ses complications.

Deux malades ont été opérés trop récemment pour classification; toutefois aucune manifestation d'activité de la tuberculose du parenchyme n'est observée. Trois malades sont "inactifs" (six à quarante-trois mois) et onze sont "stabilisés" (trois à quatorze mois). Parmi ces malades 10 au moins auraient été considérés comme incurables, à défaut de l'une ou des deux résections.

Les résections bilatérales dans la tuberculose pulmonaire sont devenues plus largement applicables sous l'influence des médications antibactériennes, qui réduisent l'incidence des complications, et des techniques chirurgicales, qui permettant la résection des segments sous-lobaires du poumon.

Les auteurs prévoient que la résection bilatérale réduira la durée de l'état de morbidité et constituera le seul moyen de cure pour un grand nombre de malades atteints de tuberculose pulmonaire.

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EXTRAPERIOSTEAL LUCITE BALL PLOMBAGE[1, 2]

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INTRODUCTION

The increasing usefulness of resection in pulmonary tuberculosis has not eliminated, but instead has altered, the scope of collapse therapy. Where applicable, excision is an effective procedure, but it cannot safely be applied except to relatively localized lesions. When excision involves dissection through planes even with well-healed lesions on both sides, complication rates rise. It is in such situations that permanent collapse therapy is indicated.

Permanent collapse therapy, as advocated by Alexander (1), has gained a well-deserved reputation. Multiple-stage thoracoplasty became the world-wide standard. Each stage was made sufficiently small so that the resulting paradoxical motion of the chest wall would not seriously handicap oxygenation and the raising of secretions. However, the mental, physical, and financial strain of a multiple-stage procedure is a paralyzing prospect to patient and physician. The cost in time and money often has resulted in delays so that many patients passed the opportune time to be helped.

Experience with these problems has led to several solutions. The object of all of the solutions is to obtain the requisite collapse of the lung in a single operation, and the principle of all is to apply a brace or prosthesis to the collapsed lung to prevent paradoxical motion, thus allowing both good ventilation and tussic force (figure 1). Extrapleural pneumothorax is such an operation. Here, the lung and overlying visceral and parietal pleura are stripped from the chest wall and braced with a prosthesis of air to prevent paradox. Oil, paraffin, Lucite spheres, and other plombages have been substituted for the air (figure 2). The pulmonary collapse is excellent; the preservation of lung function is excellent; but the danger of erosion into the lung with secondary broncho-extrapleural fistula and infection is significant (2).

It occurred to the present writers (3) and to others (4, 5, 6) independently that the interposition of an additional layer of well-vascularized tissue between the plombage and the collapsed lung might solve the problem of infection (figure 3). An extraperiosteal operation was devised, therefore, in which collapse is obtained by stripping the periosteum from the requisite ribs and inserting a plombage of Lucite balls between the denuded ribs on the outside and the periosteal beds and intercostal bundles on the inside. The periosteal beds and the spongy intercostal bundles thus act as a buffer between the collapsed lung and the plombage.

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[2] Presented before the Medical Session, as part of the symposium on *Surgery in the Treatment of Pulmonary Diseases*, at the annual meeting of the National Tuberculosis Association, Los Angeles, California, on May 21, 1953.

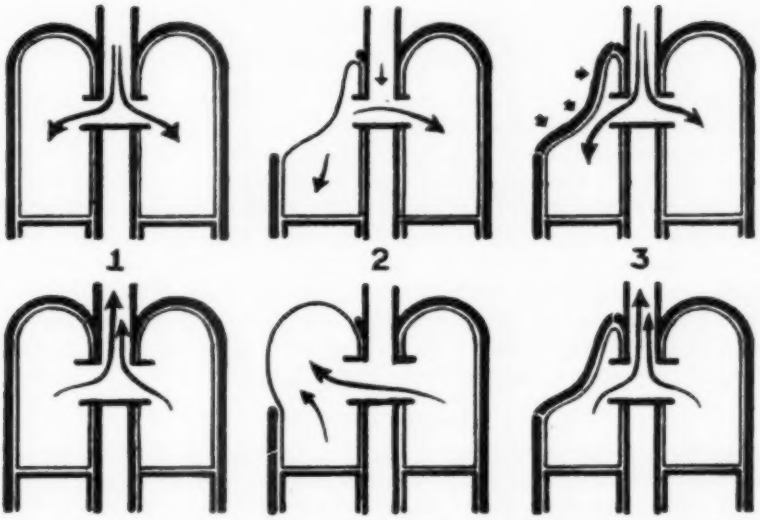

FIG. 1. Normal inspiration (above) and expiration (below) are represented on the left. The extensively decostalized chest wall allows retraction of that part of the wall with inspiration (above center) and over-expansion with expiration (below center). The underlying body of air moves back and forth within the lung and never becomes aerated. This is called paradoxical motion because the chest wall moves out when it should move in and vice versa. Any brace or prosthesis prevents paradox and restores normal exchange (No. 3 on right).

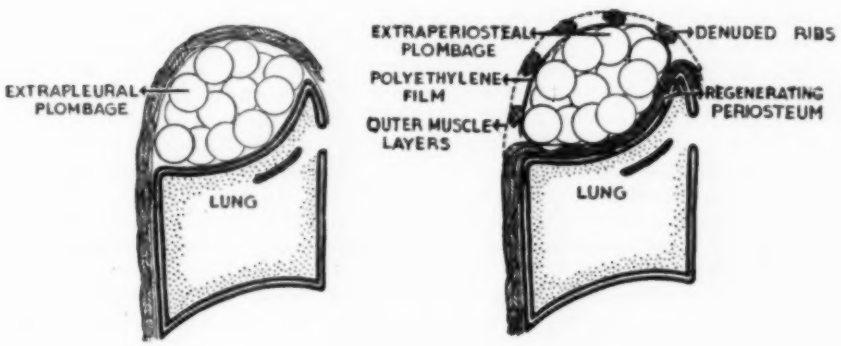

FIG. 2. (Left) *Extrapleural plombage:* Lung collapse is maintained by insertion of Lucite spheres (or other material) inside the thoracic cage. Only two layers of pleura protect the lung from erosion by the foreign body.

FIG. 3. (Right) *Extraperiosteal Lucite ball plombage:* Lucite spheres between the denuded ribs on the outside and the periosteal beds and intercostal muscles on the inside maintain lung collapse. The thick vascular layers between the lung and the foreign body prevent erosion.

OBSERVATIONS

Selection of Patients

Between December, 1948, and July 1, 1952, extraperiosteal Lucite plombage has been carried out 285 times on 270 patients. Fifteen have had bilateral plombage. The indications have varied. At first the main indication was residual cavitary disease in the apex of the lung; that is the conventional indication for thoracoplasty. Two factors have tended to change the main indication to cases of extensive and usually bilateral disease with one or more cavities in one or both apices. These are, first, the increasing safety of resection for reasonably localized lesions, and, second, the observation subsequently supported by respiratory function studies (7) that extraperiosteal plombage is far better tolerated than staged thoracoplasty. Consequently, extraperiosteal plombage has been applied more and more often as a salvage procedure in desperate-risk extensive cases.

Operative Technique

Operation is in the lateral position, usually under general anesthesia supported by transfusion. A standard periscapular incision is made and the chest wall muscles are divided and the scapula is retracted. The attachment of the serratus magnus to ribs two and three is divided. The periosteum is now stripped from the requisite number of ribs. This has varied from four to ten. As in the multi-stage thoracoplasty, the cavity location usually requires the stripping of short posterior segments of lower ribs and longer segments of upper ribs. The simplest plan is to strip the posterolateral portions from below upward through the second. Gauze is packed between denuded rib and periosteum to prevent bleeding and paradox while the posterior portions of the same ribs and the corresponding transverse processes are freed. The intercostal bundles are completely separated from the paraspinal muscles, thus allowing good collapse in the vertebral gutter. Now the anterior ends of the same ribs are deperiostealized as far forward as desired. The under surface of the first rib is next freed, thus completing the desired collapse (figure 4). The area is lavaged with saline, and a plombage of Lucite balls, 1.25 inches in diameter, is placed in the subcostal extraperiosteal space surrounded by a film of polyethylene (figure 5). Penicillin (200,000 units) and 1 gm. of streptomycin in 10 cc. of saline are placed around the plombage before routine closure of the wound in anatomic layers.

At first, due to the presence of a foreign body, occasional complicating infections were expected; and, therefore, as previously reported (3), a second stage was carried out from two weeks to six months after the first stage. The interval of time allowed the development of a sufficiently rigid plate from the periosteal beds to prevent paradoxical motion after the second operation. At this operation, the denuded ribs and the plombage were removed. Thus, a two-stage operation always attained the same end result as the multistage thoracoplasty. Because complicating infections were extremely rare, the second stage has been abandoned and the Lucite pack is left as a permanent plombage.

The first such permanent pack was done on June 30, 1949, and a total of 187 permanent plombages have been done. Infection has occurred 3 times. In none of these was erosion into the lung found, and the infection in 2 patients has been controlled by removal of the plombage and overlying ribs. The permanent plombage has the advantage of being a single-stage operation. Since no ribs are removed, there is no deformity. This is an important feature, particularly for women. Other gratifying by-products appear to be somewhat better collapse and considerably less impaired pulmonary function (7).

Extrapleural pneumonolysis is, however, somewhat better in preservation of function and should still be used when pulmonary reserve is extremely low.

FIG. 4. Drawing at operation showing the lung collapse obtained by stripping the periosteum from the ribs.

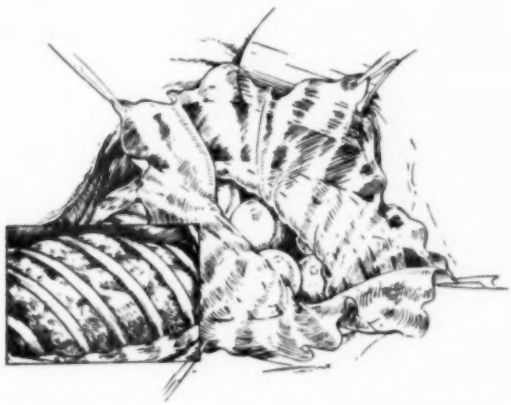

FIG. 5. The collapse is maintained and paradoxical motion of the chest wall prevented by a plombage of Lucite spheres surrounded by a polyethylene film.

Definition of Terms

Significant statistics will be presented for 285 extraperiosteal Lucite plombage operations done between December, 1948, and July, 1952. "Primary conversion" refers to patients whose sputum was rendered noninfectious and has remained so following the extraperiosteal plombage. "Secondary conversion" refers to those who required an additional operation, such as lobectomy, or a secondary course of antimicrobial agents. Sixty days was chosen arbitrarily as the postoperative period. "Tuberculous complications" are "spreads," exacerbations, empyemas, and chest wall infections due to tuberculosis.

Living patients are divided into four groups:

(*1*) Patients are listed as "clinically well and negative" if, in the opinion of the local physician, they are well, with stable chest roentgenograms and sputum negative for tubercle bacilli. Because of the wide geographic distribution of the patients, a standard evaluation of the bacteriologic and roentgenographic findings has been impossible.

(*2*) Patients who are clinically well but who may occasionally excrete tubercle bacilli in the sputum or show unstable roentgenographic findings are so designated.

TABLE 1*

AGE RANGE OF 202 TUBERCULOUS PATIENTS WHO RECEIVED EXTRAPERIOSTEAL LUCITE BALL PLOMBAGE

AGE	NUMBER OF PATIENTS
10–19	3
20–29	40
30–39	53
40–49	58
50–59	37
60 and over	11

* Statistics in tables 1 and 2 total less than the number of cases reported because these figures are not available in one group of 68 patients.

TABLE 2

DURATION OF DISEASE AND SIZE OF CAVITY IN 202 TUBERCULOUS PATIENTS WHO RECEIVED EXTRAPERIOSTEAL LUCITE BALL PLOMBAGE

DURATION OF DISEASE		SIZE OF CAVITY	
Age	Number of Patients	Size of Cavity	Number of Patients
Less than 2 years	83	4 cm. and over	54
2 to 4 years	32	Less than 4 cm.	158
4 to 6 years	25		
More than 6 years	62		

(*3*) Those with progressive disease or respiratory cripples are also so listed.

(*4*) If the most recent obtainable record is not at least as late as July, 1952, and at least six months postoperative, the case is classified "inadequate data." Thus, the period of observation varies from six months to four and one-third years.

Statistics and Results

The age range of the group of patients was seventeen to sixty-three years, with a considerable proportion among the age groups of forty and over. There were 111 males and 91 females.

Many of the older patients were males who constituted a large group of severe cases. The duration of disease and the size of the cavity (table 2) indicate the type of extensive problem which was subjected to attack.

The over-all experience is summarized in table 3. In one column the results of unilateral surgical problems (not unilateral disease) are tabulated; in the other column are the results in patients who had bilateral cavitation at the time of the first operation. Fifteen of these had bilateral extraperiosteal Lucite plombage.

TABLE 3

RESULTS IN 270 TUBERCULOUS PATIENTS WHO RECEIVED EXTRAPERIOSTEAL LUCITE BALL PLOMBAGE

	UNILATERAL, 227 CASES	BILATERAL, 43 CASES
"Primary conversion"	149 (72%)	6 (16%)
"Secondary conversion"	26 (13%)	18 (47%)
Total	175 (85%)	24 (63%)
Postoperative tuberculous complications	2 (0.8%)	3 (7%)
Late tuberculous complications	11 (4.8%)	2 (4.6%)
Total	13 (5.6%)	5 (11.6%)
Postoperative deaths	0 (0%)	2 (4.6%)
Late deaths	10 (4.4%)	5 (11.6%)
Total	10 (4.4%)	7 (16.2%)
Living	217 (95%)	36 (84%)
Clinically well, "negative" sputum	169 (78%)	22 (61%)
Clinically well, "positive" sputum or unstable roentgenogram	24 (11%)	7 (19%)
Progressive disease or respiratory cripple	3 (1.4%)	2 (6%)
Inadequate data	21 (10%)	5 (14%)

(*a*) "Bilateral" refers to patients having bilateral cavitary disease at the time of operation. Of these, 15 had bilateral Lucite plombage.

(*b*) "Primary conversion"—conversion by extraperiosteal plombage.

(*c*) "Secondary conversion"—reversal of infectiousness by secondary procedure (resection or secondary course of antimicrobial agents).

(*d*) Postoperative period—60 days.

(*e*) Status of living patients reported as percentage of living patients.

(*f*) Follow-up period: more than 6 months, 100 per cent; more than 1 year, 83 per cent; 1 year to $4\frac{1}{3}$ years, 47 per cent.

A few comments seem pertinent. The bacteriologic "conversion" rate in unilateral cases by extraperiosteal plombage alone is satisfactory, considering the severe problems. Adding "conversions" by subsequent procedure, the ultimate rate of 85 per cent is highly satisfactory. The corresponding rate of 63 per cent in bilateral cases is pleasing since these are largely salvage problems.

Tuberculous complications have not been significant. The only 2 postoperative deaths were in cases of bilateral disease. One death was apparently due to myocardial failure; and a second, to pulmonary insufficiency. Late deaths were due

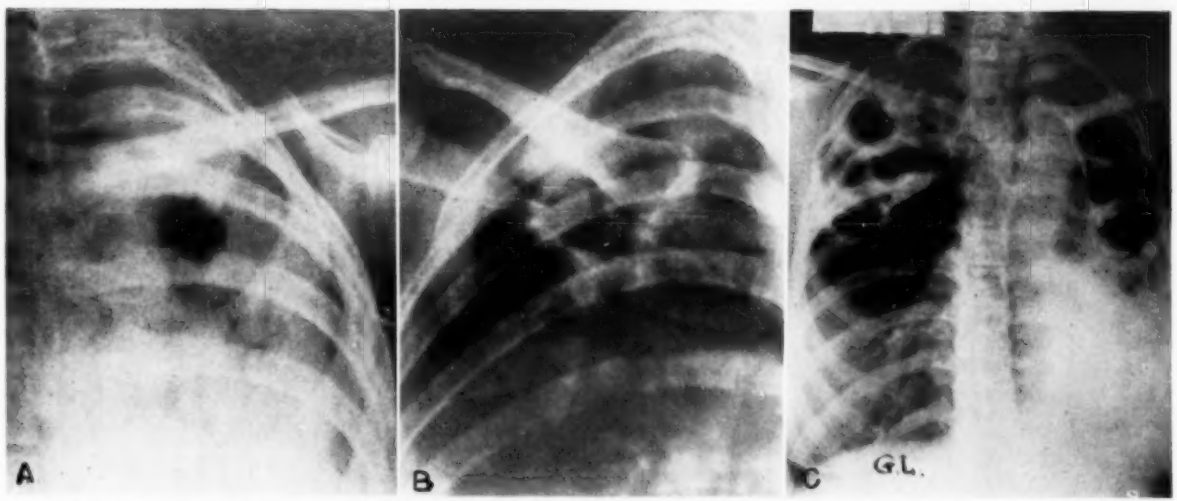

FIG. 6. *A*. Roentgenogram showing destroyed left lung of patient G. L. *B*. Cavity in right lung. *C*. After bilateral extraperiosteal Lucite plombage: sputum negative for tubercle bacilli.

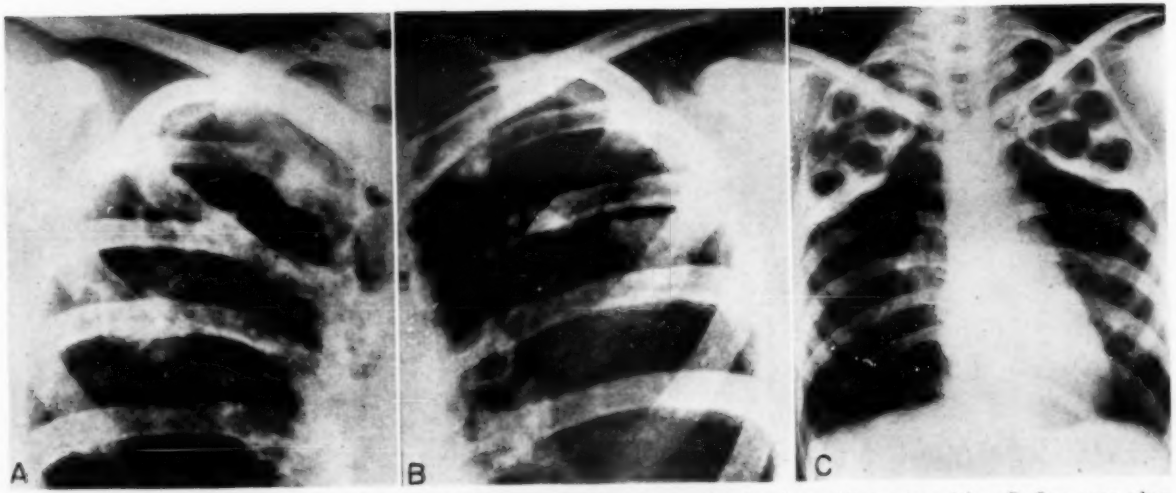

FIG. 7. *A* and *B*. Roentgenograms of right and left lungs of patient R. S., showing large bilateral cavities. *C*. One year after bilateral extraperiosteal plombage: sputum negative for tubercle bacilli. Note partial demineralization of denuded ribs.

to progressive disease (6 cases), pulmonary insufficiency (2 cases), empyema following subsequent lobectomy (1 case), and unrelated causes (6 cases).

Finally, and most important, 217 of 227 patients with unilateral surgical problems are living and, of these, 78 per cent are well and have sputum negative for tubercle bacilli. Even in the group with bilateral surgical problems, 36 of 43 are living and 61 per cent are well and have sputum negative for tubercle bacilli. Subsequent treatment is expected to increase the proportion of completely well patients.

Case Reports

Only two case reports will be presented. They represent, not the typical situation in which extraperiosteal Lucite plombage has been used, but two extreme cases of bilateral disease in which it appears to have been bilaterally successful.

Case 1. G. L., a 30-year-old white female, was first seen in January, 1951. She gave a ten-year history of cough and hoarseness and was diagnosed as having far advanced tuberculosis in 1947. Treatment was erratic because of lack of cooperation and consisted of intermittent streptomycin and para-aminosalicylic acid (PAS). Roentgenograms showed a destroyed left lung (figure 6*A*) and a large cavity at the top of the right lung (figure 6*B*). The left main stem bronchus was stenosed. A left-sided eight-rib extraperiosteal stripping with Lucite plombage was done on March 23, 1951, and was well tolerated. On May 27, 1951, a five-rib extraperiosteal stripping with Lucite plombage was done on the right (figure 6*C*). The patient's sputum was positive for tubercle bacilli on discharge from the hospital. She rested at home, had a normal pregnancy in 1952, and since leaving the hospital has had a total of twenty-one sputum examinations negative for acid-fast bacilli.[2] She is well and asymptomatic except for slight cough two years after the second operation.

Case 2. R. S., a 22-year-old white female, was seen in August, 1951, as she had far advanced bilateral pulmonary tuberculosis with large cavities of each apex (figures 7*A* and *B*). For two years she had been treated sporadically (because of poor cooperation) with rest, streptomycin, and pneumoperitoneum. She had gone through pregnancy, pyelitis, and a caesarian section. Both sputum and urine were found to be positive for acid-fast bacilli. Long-term streptomycin and PAS therapy was started. A six-rib left extraperiosteal plombage was done on September 26, 1951, and a five-rib right extraperiosteal plombage was performed on November 16, 1951 (figure 7*C*). After long-term rest and chemotherapy, the sputum and urine are now consistently negative for tubercle bacilli on culture. The patient is receiving no chemotherapy and is doing light work eighteen months after the second operation.

DISCUSSION

The operation of extraperiosteal Lucite ball plombage has proved to be a simple and safe substitute for multi-stage thoracoplasty. In addition, because pulmonary function is spared, it can be applied to advanced bilateral cases in patients in the older age group with significant amounts of cavitation, emphysema, fibrosis, or other impairments. It is effected in a single stage with no paradoxical motion of the chest wall and with no deformity. Stripping of the periosteum from the complete circumference of the ribs leads to varying degrees of demineralization but to no complications. The anticipated danger of erosions, migration of spheres, and infections around the plastic material has not developed. Fluid does develop around the plastic material in the first postoperative days but only an

[2] All smears by the Massachusetts State Laboratory.

average of one aspiration per operation is necessary. If the pleura is torn, there is usually intrapleural fluid which requires aspiration.

Attention should be focused on the large proportion of patients who are clinically well. Sputum "conversion" rates can be greatly influenced by case selection. This procedure has to a great extent been used either as a palliative procedure, with little expectation of sputum "conversion," or as a procedure planned as a preliminary to later resection. Nevertheless, 222 of the entire 244 patients on whom adequate data are available are clinically well. Undoubtedly, many of these who are clinically well but have tubercle bacilli in the sputum have good prospects for ultimate recovery.

SUMMARY

Extraperiosteal Lucite ball plombage is an easily tolerated, safe, single-stage operation to obtain permanent lung collapse in pulmonary tuberculosis. It is applicable to many extreme bilateral problems unsuitable for any other treatment. Complications are rare and end results are excellent. Broader use of extraperiosteal plombage is predicted because of its safety, simplicity, and effectiveness.

SUMARIO

Plombaje Extraperióstico con Bolas de Lucita

El plombaje extraperióstico con Lucita constituye una operación inocua y tolerada fácilmente en un solo tiempo para obtener colapso permanente del pulmón en la tuberculosis pulmonar. Es aplicable a muchos extremados problemas bilaterales que no se prestan para ningún otro tratamiento. Las complicaciones son raras y los resultados finales excelentes. Augúrase un empleo más amplio para el plombaje extraperióstico debido a su inocuidad, sencillez y eficacia.

RESUME

Plombage extrapériosté par balle de Lucite

Le plombage extrapériosté avec la Lucite est une intervention bien tolérée, sans danger, et réalisable en un temps, permettant d'obtenir le collapsus permanent du poumon dans la tuberculose pulmonaire. Il est applicable aux cas bilatéraux extrêmes auxquels aucun autre traitement ne convient. Les complications sont rares et les résultats finals excellents. Les auteurs prévoient un usage plus extensif du plombage extra-périosté, en raison de la simplicité et de l'efficacité de ce procédé.

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CHEMOTHERAPY OF MILIARY AND MENINGEAL TUBERCULOSIS IN THE ADULT[1,2]

A Report of Seventy Cases Observed Eight Months to Five Years

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INTRODUCTION

The prognosis for adult patients who develop miliary and meningeal tuberculosis is no longer hopeless. The writers have had the opportunity to treat 84 such patients during the past six and one-half years. The present report is concerned with the results in the first 70 consecutively treated patients who have been observed at least eight months to more than five years after the start of therapy. The most recent 14 cases with shorter observation periods are not included for consideration at this time.

The main purpose of the report is to present a comparison of the survival rates obtained with two different regimens of chemotherapy. No attempt will be made to review completely the voluminous literature on the subject, nor will the well-known clinical and laboratory findings in miliary and meningeal tuberculosis be discussed in any detail.

CLINICAL MATERIAL

From January 1, 1947, to September 15, 1952, 70 patients were admitted for, or subsequently developed, miliary tuberculosis, tuberculous meningitis, or both forms of tuberculous disease.

For this report the 70 patients have been divided into two series, consisting of 44 patients (*Series I*) who were started on chemotherapy between January 1, 1947, and July 1, 1950; and 26 patients (*Series II*) whose therapy was started between July 1, 1950, and September 15, 1952. The first series consisted of 12 cases of miliary tuberculosis, 22 of tuberculous meningitis, and 10 of miliary tuberculosis with the subsequent development of meningitis. The second series consisted of 6 cases of miliary tuberculosis, 13 of tuberculous meningitis, and 7 of miliary tuberculosis and tuberculous meningitis (table 1).

The over-all survival rate after eight months' observation was 25 per cent in the first series and 73.1 per cent in the second series (figure 1).

OBSERVATIONS

MILIARY TUBERCULOSIS

During the first three and one-half years, 12 patients (*Series I*) were treated for "pure" miliary tuberculosis. Their ages ranged from twenty-two to fifty years. Eleven of the 12 patients were Negro, and one was white. Eleven of the

[1] From the Tuberculosis Service, Veterans Administration Hospital, Hines, Illinois.

[2] Presented, in abstract, at the 12th Conference on Chemotherapy of Tuberculosis, Veterans Administration-Army-Navy, Atlanta, Georgia, February 10, 1953.

12 patients were acutely ill, with maximum fever ranging from 102° to 104° F.

Duration of antimicrobial therapy in this group (*Series I*) was only 120 days. Four patients received 2 gm. of streptomycin or 4 gm. of dihydrostreptomycin daily, and all of the 4 died. Of the 8 patients who received 1 gm. of streptomycin daily, 4 died and 4 have survived to date (fifty-five to sixty-four

TABLE 1

SURVIVAL RATES IN A SERIES OF SEVENTY PATIENTS WITH MILIARY, MENINGEAL, OR BOTH FORMS OF TUBERCULOSIS

	SERIES I, STARTED BETWEEN JANUARY 1, 1947 AND JULY 1, 1950 (STATUS AS OF AUGUST 15, 1950)*		SERIES II, STARTED BETWEEN JULY 1, 1950 AND SEPTEMBER 15, 1952 (STATUS AS OF MAY 15, 1953)	
	Dead	Living	Dead	Living
Miliary	8	4 (33.3%)	1	5 (83.3%)
Meningeal	19	3 (13.6%)	4	9 (69.3%)†
Miliary-meningeal	9	1 (10.0%)	2	5 (71.4%)‡
Total	36	8 (18.2%)	7	19 (73.1%)

* Status unchanged as of May 15, 1953.

† Three patients started on streptomycin plus PAS plus isoniazid—all living.

‡ Two patients started on streptomycin plus PAS plus isoniazid—both living.

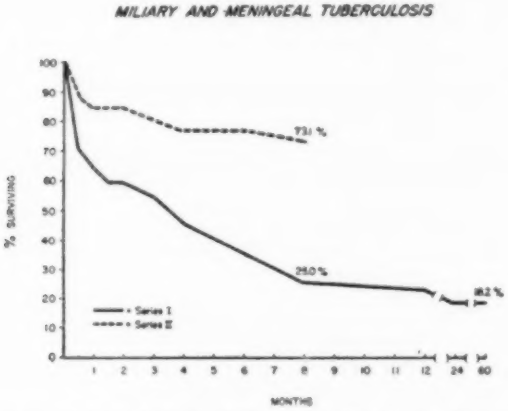

FIG. 1. Comparison of over-all survival rates of patients treated on two different regimens for miliary tuberculosis, tuberculous meningitis, and miliary-meningeal tuberculosis.

months after treatment started). Eight of the 12 patients received 4 gm. of Promin intravenously daily for fortnightly periods separated by intervals of one week without Promin. Four of the 8 who received Promin survived; whereas none of the 4 survived who did not receive Promin.

Beginning in July, 1950, the regimen of antimicrobial therapy was altered

to consist of daily streptomycin and daily para-aminosalicylic acid (PAS) to continue for a year or more. Six patients were treated for miliary tuberculosis under this regimen (table 2). Their ages ranged from thirty-one to fifty-eight years. Four of the 6 patients were Negro. All patients of this group were acutely ill with maximum fever ranging from 103° to 104° F. Two of these 6 patients received 2 gm. of streptomycin intramuscularly plus 12 gm. of PAS orally daily. The remaining 4 patients received 1 gm. of streptomycin plus 12 gm. of PAS daily. Five of these 6 patients have survived to date (eleven to twenty-three

TABLE 2

MILIARY TUBERCULOSIS—RESULTS OF COMBINED CHEMOTHERAPY
Series II—Started between July 12 and September 12, 1950

NAME	AGE	RACE	CHEMOTHERAPY	DURATION OF THERAPY	ROENTGENOGRAM IMPROVED (MILIARY ELEMENT)	REMARKS AND STATUS AS OF MAY 15, 1953
A. H.	31	N	1 gm. of streptomycin plus 12 gm. of PAS daily	6½ months	Marked	Left against medical advice at 6½ months; well at 22 months
H. B.	58	W	1 gm. of streptomycin plus 12 gm. of PAS daily	16 months	Clear	Well at 22 months
B. H.	58	N	2 gm. of streptomycin plus 12 gm. of PAS daily	27 days	—	Death on twenty-seventh day
G. G.	36	W	2 gm. of streptomycin plus 12 gm. of PAS daily	1 year	Clear	Well at 21 months
J. P.	58	N	1 gm. of streptomycin plus 12 gm. of PAS daily	6½ months	Clear	Left against medical advice at 6½ months
W. F.	32	N	1 gm. of streptomycin plus 12 gm. of PAS daily	6 months	Clear	Well at 12 months; still under therapy
			1 gm. of streptomycin twice weekly plus 12 gm. of PAS daily	6 months		

months), and one who was receiving 2 gm. of streptomycin daily died on the twenty-seventh day of therapy.

The survival rate of "pure" miliary tuberculosis after eight months' observation was 50 per cent in the first series and 83.3 per cent in the second series (figure 2). All of the 9 survivors of both series became asymptomatic and afebrile, and serial roentgenograms revealed marked to complete clearing of the miliary dissemination in all.

In the first series, one patient (R. J.) left the hospital against medical advice

after completing 120 days of treatment. Serial roentgenograms revealed moderate clearing of his miliary disease. He was readmitted in a pre-terminal state with a relapse of miliary tuberculosis and rapidly died twenty-one months after treatment was first started. Another patient (R. S.) terminated his treatment by leaving against medical advice before completing 120 days of therapy. His serial roentgenograms revealed marked clearing of miliary lesions. He was readmitted twenty-two months after treatment was originally started and quickly died from a relapse of miliary tuberculosis.

The 4 survivors of the first series have, or had, complications, suggesting that 120 days of streptomycin was inadequate therapy for miliary tuberculosis. Serial roentgenograms had *apparently* shown marked to complete clearing of

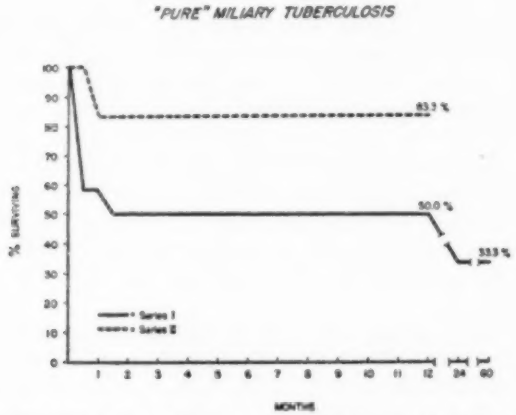

FIG. 2. In *Series I*, 2 patients left the hospital against medical advice before completing as much as four months of streptomycin therapy. Both were readmitted in extremis and died 21 and 22 months, respectively, after treatment was originally started. In *Series II*, one patient died on the twenty-seventh day of therapy. His bacilli were completely resistant to streptomycin before treatment was started.

the miliary lesions. However, one patient (H. M.) left the hospital against medical advice twice; three and one-half years later, he had disseminated nodular tuberculosis, which probably represented exacerbation of miliary lesions which seemed to have cleared markedly during his original course of treatment. All of the 4 survivors, including the latter patient (H. M), developed tuberculous epididymitis within seven to twenty-one months after discontinuation of chemotherapy. One of these 4 patients (W. L.) also developed osseous tuberculosis, tuberculous abscesses and sinuses.

In the second series, 2 survivors (J. P. and A. H.) terminated treatment by leaving the hospital against medical advice after six and one-half months of therapy and were clinically well at eighteen months and twenty-two months, respectively, after treatment was originally started. Two survivors (G. G. and

H. B.) completed treatment of one year and sixteen months respectively, and one (W. F.) was in his thirteenth month of treatment. One of the 5 survivors of this series developed tuberculous epididymitis four months after completing a sixteen-month course of chemotherapy. None has shown a relapse of miliary tuberculosis to date (eleven to twenty-two months since start of therapy).

TUBERCULOUS MENINGITIS

Prior to July 1, 1950, it was the policy at this institution to treat tuberculous meningitis with one course of 2 gm. of streptomycin intramuscularly daily for 120 days, with a few exceptions hereinafter noted. In the majority of cases, 50 mg. of streptomycin were also given intrathecally three times weekly. However, only one patient of this group (*Series I*) received intrathecal streptomycin after May, 1948. During this period, 22 patients (*Series I*) were treated for "pure" meningitis. The diagnosis of tuberculous meningitis was confirmed bacteriologically or on post-mortem examination in 19 of the 22 patients (86.4 per cent). Nine patients were Negro, and 13 were white; their ages ranged from nineteen to fifty-eight years. Only 3 patients of this group survived one year, and all of the 3 were living five years after the start of treatment.

Fifteen of the 19 fatalities occurred within the first three and one-half months of therapy, and 8 of the 15 died within the first month. Only 7 of the 22 patients survived long enough to complete 120 days of treatment. Two of these 7 patients were treated continuously for six months, and both survived. Treatment was terminated at 120 days in 5 of the 7 patients. One of the 5 survived, and 4 relapsed and died.

Thirteen of the 22 patients received 50 mg. of streptomycin intrathecally thrice weekly, and one survived. Nine of the 22 patients did not receive streptomycin intrathecally, and 2 survived. Ten of the 22 patients received Promin, and 3 survived (2 of the 3 survivors received streptomycin intramuscularly for six months); whereas there were no survivors among the 12 patients who did not receive Promin.

During the past two and one-half years, 13 patients (*Series II*, table 3) were treated for "pure" tuberculous meningitis. The diagnosis of tuberculous meningitis was confirmed bacteriologically in 10 of the 13 patients. Therapy for this group was modified by prolonging the original course of streptomycin to at least nine months, adding at least 12 gm. of PAS daily (or sodium PAS in equivalent amounts), omitting intrathecal therapy in all but one case, and adding 450 mg. of isoniazid daily to the dosage in 3 cases started between June and September 15, 1952. In those patients who were in coma, or unable to swallow, PAS was given parenterally in doses of 12 to 20 gm. daily until oral medication became feasible. Nine of the 13 patients were Negro; their ages ranged from twenty-six to sixty years. The detailed relationship of therapy to survival rates is shown in table 3.

Four of these 13 patients died (30.7 per cent) and 9 (69.3 per cent) have survived to date (eight to thirty-four months). (The survival rate in our first series was 18.2 per cent at the end of eight months, figure 3.) Two of the 4 fatalities occurred on the first and eighth days of therapy; another patient, whose bacilli

TABLE 3

TUBERCULOUS MENINGITIS—RESULTS OF COMBINED CHEMOTHERAPY

Series II—Started between July 12, 1950, and September 12, 1953

NAME	AGE	RACE	CHEMOTHERAPY	DURATION OF THERAPY	REMARKS AND STATUS AS OF MAY 15, 1953
J. F.	50	N	1 gm. of streptomycin daily 2 gm. of streptomycin plus 12 gm. of PAS daily	1 month 12 months	Operative tuberculoma premeningitis; post-operative hemiplegia; well at 34 months
P. P.	58	W	2 gm. of streptomycin plus 12 gm. of PAS daily	1 day	Previous corticotropin therapy; death first day of therapy
L. C.	43	N	2 gm. of streptomycin plus 12 gm. of PAS daily	12 months	Discharged
			1 gm. of streptomycin twice weekly plus 12 gm. of PAS daily	12 months	Well at 29 months
N. G.	39	N	2 gm. of streptomycin daily 2 gm. of streptomycin plus 12 gm. of PAS daily	1 month 12 months	Well at 20 months
			1 gm. of streptomycin plus 12 gm. of PAS daily	11 months	Still under therapy
Mo. C.	28	W	2 gm. of streptomycin plus 12 gm. of PAS daily	74 days	Death seventy-fourth day of therapy; resistant to 100 γ streptomycin per ml.
W. B.	26	N	2 gm. of streptomycin plus 12 gm. of PAS daily	9 months	Left against medical advice 1 month during therapy; well at 18 months
W. S.	37	W	2 gm. of streptomycin plus 12 gm. of PAS daily	6 months	Well at 15 months
			1 gm. of streptomycin plus 12 gm. of PAS daily	6 months	Left against medical advice at 12 months
J. H.	39	N	2 gm. of streptomycin plus 12 gm. of PAS daily	6 months	Well at 14 months
			1 gm. of streptomycin plus 12 gm. of PAS daily	8 months	Still under therapy
W. F.	40	N	2 gm. of streptomycin plus 30–12 gm. of PAS daily	4 months	Responded well before leaving against medical advice; death at home 2½ months later
M. E. C.	54	W	2 gm. of streptomycin plus 12 gm. of PAS daily	8 days	Death eighth day of therapy
M. Cl.	34	N	2 gm. of streptomycin plus 20–12 gm. of PAS plus 450 mg. of isoniazid daily	11 months	Well at 11 months; still under therapy
J. L.	31	N	2 gm. of streptomycin plus 12 gm. of PAS daily	1 month	Well at 12 months
			1 gm. of streptomycin plus 12 gm. of PAS plus 450 mg. of isoniazid daily	11 months	Still under therapy
G. B.	60	W	2 gm. of streptomycin and 12 gm. of PAS plus 450 mg. of isoniazid daily	8 months	Well at 8 months; still under therapy

were completely resistant to streptomycin when therapy was started, died on the seventy-fourth day. The fourth fatality (W. F.) occurred in a patient who terminated his treatment by leaving against medical advice after four months of therapy. He died two and one-half months after leaving this hospital. He was responding well clinically, and his cerebrospinal fluid findings were approaching normal (cells, 12 per cu. mm.; protein, 39.5 mg.; sugar, 75 mg. per 100 ml.) when he left the hospital. It is believed that he had a good chance of surviving had he continued on therapy for at least a year or more. He was the only patient of the second series to develop a relapse of tuberculous meningitis.

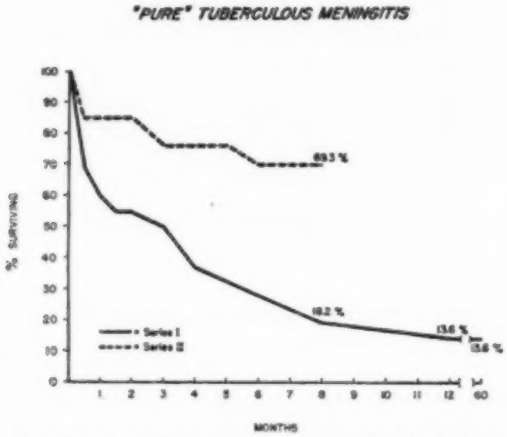

FIG. 3. In *Series II*, 2 patients died on the first and eighth days of therapy. One patient died on the seventy-fourth day of therapy. His bacilli were completely resistant to 100 γ of streptomycin per ml. before treatment for meningitis was started. The fourth fatality was a patient who left the hospital against medical advice four months after treatment was started, at which time his cerebrospinal fluid findings were nearly normal. He died outside of this hospital two and one-half months later.

Duration of symptoms of tuberculous meningitis, before treatment was started, was three days to twelve weeks (average three weeks) in the first series and three days to fourteen weeks (average four weeks) in the second series.

Stigmata and Sequelae of Tuberculous Meningitis

Of the 3 survivors of the first series, one has slight right drop foot (W. D.), one has marked impairment of vision (J. C.), and one has no sequelae of meningitis. Of the 9 survivors of the second series, one has slight atrophy of the left deltoid and shoulder muscles and partial deafness (J. H.); one has mental deficiency and mild right hemiplegia, which are both attributed to operation for tuberculoma (J. F.); one has mental retardation, complete deafness, and weakness of extra-ocular muscles (N. G.); one has borderline mental deficiency (W. B.); and 5 show no sequelae of meningitis to date. Marked vestibular damage was present in all survivors.

Cerebrospinal Fluid Findings in Tuberculous Meningitis

Exclusive of bacteriologic studies for confirmation of the diagnosis, most information was derived from serial determinations of the total protein, glucose concentration, and cell counts of the cerebrospinal fluid. At one time or another, all of the patients had high protein content, low glucose concentration, and elevated cell count. In all survivors, the glucose concentration returned to normal within two months. Cell counts returned to normal within four months in most survivors and within eight months in all. The protein content was usually last to return to normal levels and, in one case (L. C.), it was 150 mg. per 100 ml. at the end of two years of continuous treatment.

The writers insisted upon there being normal sugar levels and cell counts for at least six months before considering termination of therapy. It is preferable, moreover, to continue treatment until the protein content is also within normal limits or at least consistently falling during a course of eighteen or more months of treatment.

COMBINED MILIARY AND MENINGEAL TUBERCULOSIS

During the first three and one-half years (*Series I*), 9 of 10 patients treated for combined miliary and meningeal tuberculosis died within four and one-half months after the onset of meningitis. Six of the 9 fatalities occurred within two and one-half months after the onset of meningitis. Only one (J. J.) survived to date (sixty-four months). The diagnosis of tuberculous meningitis was confirmed bacteriologically in 8 of the 10 patients, and the lone survivor was one of the 8 proved cases.

Maximum duration of antimicrobial therapy in this group was 120 days, with one exception (J. J.). Six of the 10 patients received Promin, and 5 of the 10 patients received streptomycin intrathecally. The sole survivor received Promin intravenously and streptomycin intramuscularly and intrathecally. He was the only patient to receive a second four-month course of therapy shortly after the first course was completed. Clinically he responded well to chemotherapy, and serial roentgenograms revealed complete clearing of the miliary lesions. He developed tuberculous epididymitis nearly two years later. This patient shows no sequelae of meningitis. He continues to have epilepsy which was present before he developed miliary and meningeal tuberculosis.

During the subsequent two and one-half years (*Series II*, table 4), 5 of the 7 patients (71.4 per cent) with combined miliary and meningeal tuberculosis survived to date (eight to thirty-four months). (The survival rate in the first series was 10.0 per cent at the end of eight months, figure 4). One patient died on the second day of treatment. Another died on the forty-ninth day of therapy for meningitis following several severe gastrointestinal hemorrhages and in spite of transfusions of three liters of blood. Two days prior to death, this patient's cerebrospinal fluid findings were approaching normal (cells, 9 per cu. mm.; protein, 63 mg.; and sugar, 66 mg. per 100 ml.). This patient did not tolerate PAS because of a peptic ulcer.

The diagnosis of tuberculous meningitis was confirmed bacteriologically in 6 of the 7 patients. The seventh patient (J. B.) presented typical clinical, roent-

TABLE 4

COMBINED MILIARY-MENINGEAL TUBERCULOSIS—RESULTS OF THERAPY

Series II—Started between July 12, 1950, and September 12, 1952

NAME	AGE	RACE	CHEMOTHERAPY	DURATION OF THERAPY	THERAPY FOR	ROENTGENOGRAPHIC IMPROVEMENT (MILIARY)	REMARKS AND STATUS AS OF MAY 15, 1953
H. H.	58	W	1 gm. streptomycin twice weekly plus 12 gm. PAS daily	8 months*	Miliary	Marked	Developed meningitis two months after therapy stopped; in coma 4 months; sequelae severe
			2 gm. streptomycin plus 12 gm. PAS daily	10½ months	Meningitis		
J. S.	27	N	1 gm. streptomycin (intolerant of PAS) daily	55 days*	Miliary		Admitted tuberculosis service fifty-fifth day of therapy; death from gastrointestinal hemorrhage
			2 gm. streptomycin daily	49 days	Meningitis		
L. H.	36	N	2 gm. streptomycin plus 20 gm. PAS daily	2 days	Both		Death on second day of therapy
R. B.	30	N	2 gm. streptomycin plus 12 gm. PAS daily	17 months	Both	Marked	Still under therapy; clinically well
J. B.	49	N	2 gm. streptomycin plus 12 gm. PAS daily	32 days*	Miliary	Marked	Developed meningitis; transferred; left against medical advice 2 months later; well at 8 months
			2 gm. streptomycin plus 12 gm. PAS daily	27 days	Meningitis		
J. G.	26	N	1 gm. streptomycin daily	35 days*	Miliary	Marked	Admitted to tuberculosis service thirty-fifth day of therapy; developed meningitis; still under therapy
			2 gm. streptomycin plus 12 gm. PAS daily plus 450 mg. isoniazid	8 months	Meningitis		
C. W.	30	N	1 gm. streptomycin plus 12 gm. PAS daily	8 months*	Miliary		Developed meningitis late (ninth month of therapy); meningitis responding well to present therapy
			1 gm. streptomycin twice weekly plus 12 gm. PAS daily	1 month*	Miliary		
			2 gm. streptomycin plus 12 gm. PAS daily plus 600 mg. isoniazid daily	8 months	Meningitis		

* Period of treatment for miliary tuberculosis before onset (or diagnosis) of meningitis.

genographic, and laboratory findings of miliary tuberculosis and tuberculous meningitis. Serial roentgenograms revealed marked clearing of miliary dissemination in 5 of the 7 patients. Roentgenograms were not available for comparison in the 2 fatal cases.

All of the 5 survivors responded well to treatment and became free of clinical findings of active meningitis; and the cerebrospinal fluid findings were normal in the 4 patients who remained under observation. One of the 4 patients completed treatment fifteen months ago, and 3 were still under treatment. The fifth survivor was transferred to a local hospital on the twenty-seventh day of therapy and continued to do well. He left that hospital against medical advice after a total of three and one-half months of treatment (probably sacrificing a potentially

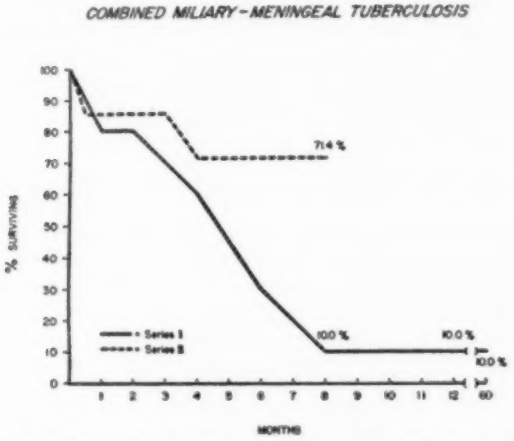

FIG. 4. Of the 2 fatalities in *Series II*, one patient died on the eighth day and the other on the forty-ninth day of therapy for complicating meningitis. The immediate cause of death in the latter case was massive hemorrhage from a large gastric ulcer. One day before his death, cerebrospinal fluid findings were nearly normal.

good prognosis). He was still clinically well eight months after treatment was originally started. None of the 4 survivors of the second series, still under observation, has developed tuberculous epididymitis since starting chemotherapy and none has experienced a relapse.

As stated previously, it should be emphasized that the changes in therapy applicable to the patients in the second group were: prolongation of basic streptomycin therapy, the addition of at least 12 gm. of PAS daily (or its equivalent in sodium PAS), the omission of intrathecal streptomycin, and the addition of 450 to 600 mg. of isoniazid daily to 2 patients who were started on therapy in June and September, 1952.

The duration of miliary tuberculosis before the onset of meningitis was three to twelve weeks in the first series and four weeks to nine months in the second

series. The complication of meningitis was treated within one to three days after meningeal symptoms were noted in both series. In the first series tuberculous meningitis developed in 10 of 22 patients (45.5 per cent) while they were receiving chemotherapy for miliary tuberculosis. It is quite probable that the onset of meningitis was subdued and the diagnosis delayed for some period of time in a number of these cases. In the second series, tuberculous meningitis developed in 2 (J. S. and C. W.) of 8 patients (20 per cent) while they were receiving chemotherapy for miliary tuberculosis; and a third patient (H. H.) developed tuberculous meningitis two months after premature termination of inadequate therapy for miliary tuberculosis. The diagnosis of combined miliary-meningeal tuberculosis was made on admission in 3 cases (R. B., J. B., and J. G.) of the second series.

In the case of one patient (C. W.), streptomycin was reduced to 1 gm. twice weekly at the end of nine months of therapy; he developed tuberculous meningitis six weeks later. He appears to be responding well to treatment with 450 mg. of isoniazid daily plus 2 gm. of streptomycin and 12 gm. of PAS daily. At present, the writers are reluctant to reduce the dosages of the drugs employed within the first year of therapy.

Stigmata and Sequelae of Miliary-Meningeal Tuberculosis

The one survivor of the first series has no sequelae due to miliary-meningeal tuberculosis. Of the 4 survivors in the second series who are still under observation, one has impaired vision in one eye (J. G.), one shows severe brain damage (H. H.), and 2 have no sequelae.

Discussion

A detailed analysis of the clinical manifestations of miliary and meningeal tuberculosis has purposely been omitted from the present report, for the literature is replete with adequate discussions of this phase of the subject. The case material of both series is comparable in age, sex, race, and severity and duration of illness before chemotherapy was started. The clinical, roentgenographic, and laboratory findings were similar to those previously reported (1). Other forms of tuberculosis were present in the majority of patients of both series before the onset of miliary and meningeal tuberculosis. These associated forms of tuberculosis usually improved in those patients who survived.

The present discussion is directed primarily to the survival rates of patients who received chemotherapy for miliary tuberculosis, tuberculous meningitis, and combined miliary-meningeal tuberculosis. The gross survival rates in the second series of patients were considerably better than in the first series (table 1). Prior to July 1, 1950, all patients with these forms of tuberculosis received original courses of streptomycin, alone or with Promin, for 120 days, with the 4 exceptions already noted. Even in the first series, 3 of the 4 (W. K., W. D., J. B., and J. J.) who received six or more months of therapy have survived to date. Since July 1, 1950, the therapeutic program has consisted of streptomycin intramuscularly plus PAS for at least a year or more; and since June, 1952,

isoniazid has been added. Only one patient in the second series received streptomycin intrathecally.

The survival rate of patients with "pure" miliary tuberculosis was 33.3 per cent in the first series and 83.3 per cent in the second. As previously noted, the changes of therapy for the second series were the prolongation of streptomycin administration and the addition of PAS. The addition of isoniazid is also recommended in any new case of miliary tuberculosis, with the hope of avoiding the development of tuberculous meningitis. It seems likely that prolonged, continuous chemotherapy with streptomycin plus PAS plus isoniazid will aid in the control of residual miliary foci and diminish the incidence of meningitis. It is of considerable importance to obtain regular periodic examinations of the cerebrospinal fluid of all patients who are receiving chemotherapy for miliary tuberculosis, even in the absence of any suggestion of central nervous system involvement. The onset of meningitis may be masked, delayed until very late, or even overlooked in patients who are receiving chemotherapy for other forms of tuberculosis; and this is particularly true of miliary tuberculosis. In some instances, tubercle bacilli have been cultured from cerebrospinal fluid specimens which were otherwise normal (F. McC., F. Fl., J. S.).

The gross survival rate of patients with "pure" tuberculous meningitis was 13.6 per cent in the first series as compared with 69.3 per cent in the second. In the second series, prolonging streptomycin therapy and adding PAS raised the survival rate to 60 per cent; and, since adding 450 mg. of isoniazid daily, the survival rate has been 100 per cent (only 3 patients). The writers continue to be encouraged by the early response of another 12 patients with "pure" tuberculous meningitis started on treatment within the past eight months and to be reported on later. Early reports of McDermott and his associates (2), Lepper (3), Tempel (4), and others would indicate that the addition of isoniazid holds promise for even better recovery rates, fewer relapses, and a lessened incidence of meningitis developing in patients under treatment for miliary tuberculosis.

The gross survival rate of patients with combined miliary-meningeal tuberculosis was 10.0 per cent in the first series and 71.4 per cent in the second. In the second series, prolonging streptomycin therapy and adding PAS raised the survival rate to 50 per cent; and, since adding 450 mg. of isoniazid daily, the survival rate has been 100 per cent (only 2 patients). Three recent cases, not included in this report, also appear to be responding well.

Summary

The survival rates of 70 patients who were treated for miliary tuberculosis, tuberculous meningitis, and combined miliary-meningeal tuberculosis and observed for periods of at least eight months to more than five years are reported.

The 70 patients were divided into two series consisting of 44 patients who were started on chemotherapy during the first three and one-half years (*Series I*) and 26 patients who were started during the next two and one-quarter years (*Series II*) of the study.

Survival rates were considerably higher for the second series at comparable periods of observation.

It is believed that the prolongation of the original course of chemotherapy and the addition of para-aminosalicylic acid (PAS) contributed materially to the superior early results in the second series of cases. Since the addition of isoniazid, the results have been even better.

The writers are not convinced that the intrathecal administration of streptomycin is necessary in the treatment of tuberculous meningitis since intrathecal therapy did not appear to favorably influence the survival rates even before the advent of isoniazid.

Current results suggest that even better survival rates may be attained, providing the "original" course of adequate therapy (streptomycin plus PAS plus isoniazid) is started early, given continuously, and is sufficiently prolonged.

Sumario

Quimioterapia de la Tuberculosis Granúlica y Meníngea en el Adulto. Presentación de Setenta Casos Observados de Ocho Meses a Cinco Años

Preséntanse las tasas de sobrevivencia de 70 enfermos que fueron tratados por granulia, tuberculosis meníngea y granulia y tuberculosis meníngea combinadas y mantenidos en observación durante períodos a lo menos de ocho meses hasta más de cinco años.

Los 70 sujetos fueron divididos en dos series, constando de 44 enfermos en quienes se inició la quimioterapia durante los primeros tres años y medio (*Serie I*) y 26 enfermos en quienes se inició el tratamiento durante los siguientes dos años y cuarto (*Serie II*) del estudio.

Las tasas de sobrevivencia fueron considerablemente mayores para la segunda serie en épocas comparables de observación.

Opinan los AA. que la prolongación de la primitiva serie de quimioterapia y la agregación de ácido para-aminosalicílico (PAS) contribuyeron decididamente a los superiores resultados tempranos en la segunda serie de casos. Desde que se agregara isoniacida, los resultados han sido aun mejores.

No se sienten convencidos los AA. de que la administración intratecal de estreptomicina es necesaria en el tratamiento de la meningitis tuberculosa, dado que la terapéutica intratecal no pareció afectar favorablemente las tasas de sobrevivencia ni aun antes de la introducción de la isoniacida.

Los resultados actuales sugieren que pueden obtenerse hasta mejores tasas de sobrevivencia, con tal que la serie "primitiva" de terapéutica adecuada (estreptomicina más PAS más isoniacida) sea iniciada tempranamente, administrada continuamente y prolongada suficientemente.

Resume

Chimiothérapie de la tuberculose miliaire et méningée de l'adulte. Rapport sur soixante-dix cas pendant des périodes d'observation de huit mois à cinque années

Les auteurs communiquent les taux de survie de 70 sujets traités pour tuberculose militaire méningée tuberculeuse et tuberculose méningo-miliaire, observés pendant des périodes allant d'un minimum de huit mois à cinq ans.

Les 70 malades ont été répartis en deux groupes. La chimiothérapie a été instaurée au cours des premiers trois ans et demi de l'étude chez 44 malades (*série I*) et chez 26 malades au cours des deux ans et quart suivants (*série II*).

Les taux de survie obtenus étaient considérablement plus élevés dans la second série, les durées d'observation étant comparables.

Les auteurs pensent que la prolongation de la chimiothérapie originale avec association d'acide para-aminosalicylique (PAS) a contribué matériellement aux résultats supérieurs

obtenus dans la deuxième série des cas. Depuis l'adjonction de l'isoniazide, les résultats sont encore améliorés.

Le auteurs ne sont pas convaincus que l'administration sous-arachnoïdienne de la streptomycine soit nécessaire dans le traitement de la méningite tuberculeuse car, même avant l'introduction de l'isoniazide, le traitement par voie sous-arachnoïdienne ne paraissait pas influencer favorablement les taux de survie.

Les résultats actuels permettent de supposer qu'il sera possible d'atteindre des taux de survie encore meilleurs lorsque le traitement "original" adéquat (streptomycine plus PAS plus isoniazide) est instauré précocement, donné continuellement et prolongé suffisamment.

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A COMPARISON OF TRACHEAL AND GASTRIC LAVAGE IN THE CULTURING OF M. TUBERCULOSIS[1]

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INTRODUCTION

A new method of culturing *M. tuberculosis* from patients with pulmonary tuberculosis was devised by de Abreu in 1944 (1). It was termed pulmonary lavage and the transglottic approach was utilized. Somewhat later in the same year, Fernandes introduced the supraglottic method and called the procedure tracheobronchial lavage (2). The terms bronchial and tracheal lavage have also been employed and the latter seems preferable. The techniques as described by the various operators differ slightly in the depth of anesthesia obtained and in the way in which water or saline is introduced into the tracheobronchial tree (3–6). Anesthesia varies from none at all to a state in which the cough reflex is abolished and the patient must voluntarily cough up the water. Sterile saline or water is introduced via a metal cannula by some, through a catheter passed down almost to the carina by others, while still others drip the solution over the posterior aspect of the tongue.

In 1948, Bueno summarized the results of eleven studies in which a comparison was made between the tracheal and the gastric lavage in terms of the numbers of cultures of *M. tuberculosis* obtained (5). In all but three of these studies, a higher percentage of cultures positive for tubercle bacilli was obtained by the use of the tracheal lavage. The advantages of the procedure were as follows: The technique of the tracheal lavage is easier for the physician, can be done at any time, and is better tolerated by the patient. The patient cannot deceive the doctor as he can with a gastric lavage. The tubercle bacilli are not destroyed after the specimen is obtained as they may be in gastric juice when stomach washings are not properly prepared.

One hundred and ninety-nine patients were studied by Wardrip, Scarborough, and Roberts, all of whom had sputum negative for acid-fast bacilli on examination of the direct smear (6). In 111 of these patients, cultures positive for tubercle bacilli were obtained on tracheal lavage; of these 111 patients, 86 also had a gastric lavage and in only 24 cases was the culture positive for tubercle bacilli; in no case was the gastric lavage positive for tubercle bacilli in the presence of a "negative" tracheal lavage. Tracheal lavage was preferred by these investigators for the following reasons: The material to be cultured is obtained closer to the source of its origin and has not been diluted or dissipated; the bacilli have not had their viability impaired by coming in contact with gastric acid and enzymes; it is not necessary to do a tracheal lavage on a fasting stomach; and tracheal lavage is well tolerated by the patient.

Staines did a bronchial lavage on 382 persons who previously had been found to have negative sputum and gastric content examinations for *M. tuberculosis*. In 99 of these cases in which tuberculosis was suspected, tubercle bacilli were cultured in 24.2 per cent; in 208 patients with known tuberculosis, being studied to determine the activity of the disease, bacilli were cultured in 14.9 per cent; and in 75 instances

[1] From the Bret Harte Sanatorium, Murphys, California.

in which nontuberculous chest disease had been diagnosed, tubercle bacilli were obtained in 4 per cent. Staines considers bronchial lavage to be preferable to gastric lavage because of its simplicity, reliability, and slight discomfort to the patient (7).

With the exception of three of the eleven studies summarized by Bueno, none was found in the literature which did not show a higher percentage of positive cultures of tubercle bacilli with tracheal than with gastric lavage.

METHODS AND MATERIAL

In order to evaluate the effectiveness in obtaining tubercle bacilli on culture of gastric lavage, as done by the staff at Bret Harte Sanatorium, 463 patients have been studied between April 1, 1951, and April 1, 1953.

When the study was first begun, cases were selected at random, but within a short time it was decided to limit the tests to those patients whose sputum cultures were negative for tubercle bacilli.

Gastric lavage was done in the usual manner by a laboratory technician, the patient being brought to the laboratory in a wheelchair or allowed to walk, if ambulatory, immediately upon arising. If it had been feasible to have the gastric lavage done at the patient's bedside, it is probable that an even higher percentage of positive lavages would have been obtained with this technique.

Within a maximum of thirty, and usually within fifteen, minutes after the lavage was done, the gastric contents were prepared as follows: to the specimen, a small amount of caroid (a muco-solvent) was added and the mixture was incubated for thirty minutes with occasional agitation; 4 per cent sodium hydroxide in an amount equal to the volume of the specimen plus two drops of phenol red were then added. This was mechanically shaken for fifteen minutes and then neutralized to a pH of 6.8 with 10 per cent hydrochloric acid; the specimen was then concentrated by centrifuging for ten minutes at 1,500 r.p.m., and smears and cultures were made immediately on Löwenstein-Jensen medium.

Tracheal lavage was done by one of the staff physicians either on the same day as the gastric lavage, usually immediately following it, or on the next day. In some cases an attempt was made to introduce the sterile water into the tracheobronchial tree without first anesthetizing the throat, but it was usually found to be impossible to obtain a good specimen without using topical anesthesia. Therefore, in the majority of the patients, the posterior tongue, tonsillar pillars, and pharynx were first anesthetized with 2 per cent Pontocaine, the technique being the same as that used in preparing a patient for bronchoscopy except that no Pontocaine was injected into the larynx. The anesthetic was first sprayed into the throat with an atomizer and then a few minutes later was painted on the tongue and neighboring structures with a brush. When adequate anesthesia was obtained, 5 cc. of sterile water were introduced blindly into the trachea by means of a syringe with attached metal cannula. Only in a very few cases was it done under direct visualization with a head mirror. In each case, regardless of which method of introducing the water was used, an attempt was made to obtain a good cough with flecks of mucus in the resultant specimen. Usually, a total of 20 to 25 cc. of water was needed.

The specimen was prepared by adding an equal volume of 4 per cent sodium hydroxide plus four drops of phenol red. The mixture was then allowed to stand for two hours with occasional agitation, neutralized to a pH of 6.8 with 10 per cent hydrochloric acid, and concentrated by centrifuging for ten minutes at 1,500 r.p.m. Smears were made and cultures were inoculated on Löwenstein-Jensen medium.

In doing a tracheal lavage, the operator wears mask, cap, gown, gloves, and a plastic face shield.

RESULTS

A total of 486 gastric and 486 tracheal lavages were done. They were done more than once on the same patient on 23 occasions. Because of the possible presence on nonpathogenic acid-fast bacilli in the stomachs of many persons, and because of the possible presence of killed but nonautolyzed tubercle bacilli in the equipment used, the significance of the finding of acid-fast bacilli in a smear of concentrated gastric content has been questioned (8). Therefore, only the results of the cultures will be considered in attempting to decide which is the more sensitive method for detection of *M. tuberculosis*, the gastric or the tracheal lavage. It is interesting to note, however, that in only 4 cases was the gastric smear positive for acid-fast bacilli, with the culture being negative for tubercle bacilli. Moreover, in 3 of these instances, the tracheal smear was also positive while the culture was negative. All 3 of these patients were receiving extensive chemotherapy at the time of the tests, and all had "positive" cultures of sputum or gastric lavage material at a later date.

TABLE 1

RESULTS OF CULTURES FOR M. TUBERCULOSIS OF SPECIMENS OBTAINED BY GASTRIC AND BY TRACHEAL LAVAGE

NUMBER OF PATIENTS*	TRACHEAL LAVAGE	GASTRIC LAVAGE
345	Negative	Negative
100	Positive	Positive
29	Negative	Positive
12	Positive	Negative

Total positive with gastric lavage: 129 (26.56 per cent).
Total positive with tracheal lavage: 112 (23.05 per cent).
* Tests done two times on 23 patients.

In 345 cases, both tracheal and gastric lavage cultures were negative for *M. tuberculosis*. In 100, both were positive, and in 41 the findings were in disagreement. In 29 of the 41, the gastric culture was "positive," the tracheal being "negative"; in 12, the tracheal was "positive," the gastric being "negative." A total of 129 patients (26.56 per cent) yielded cultures positive for tubercle bacilli on gastric lavage, and 112 (23.05 per cent) yielded "positive" cultures on tracheal lavage (table 1).

Because of these results, the writers cannot agree with opinions in the literature that cultures of tracheal lavage material are too sensitive a method to be used as a guide to the change or discontinuation of therapy (6).

Among this group of 41 patients whose cultural findings by the two methods were in disagreement, 18 were classified as having minimal, 17 as moderately advanced, and 6 as far advanced, pulmonary tuberculosis. More than twice as many minimal cases had gastric cultures positive for tubercle bacilli, the tracheal being negative, than vice versa (table 2).

Although in the present series a greater number of cultures positive for tubercle bacilli were obtained with the gastric lavage than with the tracheal, the difference

was not statistically significant. It is believed that, from the the standpoint of diagnostic accuracy alone, neither method is to be given preference over the other. There are a number of other factors to be considered, however, if a choice must be made between the two techniques, and these factors will subsequently be discussed.

The possibility of spread of tuberculosis in the lungs following tracheal lavage has been suggested by a number of writers (10, 11). Although the present writers prefer gastric lavage for routine use, this is not one of the reasons for the preference. It was impossible to review the roentgenograms of all the patients who had had tracheal lavages. The films of only those patients who had been examined during the first six months of 1952 with a roentgenogram at least two months, and no longer than four months, after the lavage were reviewed from this standpoint. Roentgenograms of 54 such patients, including 17 with minimal, 23 with moderate, and 14 with far advanced, pulmonary tuberculosis were studied. The roentgenogram immediately preceding the lavage was compared with the one following it by at least two members of the staff. Chest roentgenograms of an equal number of patients with comparable amounts of disease and who were

TABLE 2

CLASSIFICATION OF TUBERCULOSIS OF 41 PATIENTS IN WHOM CULTURAL FINDINGS OF GASTRIC AND TRACHEAL LAVAGES WERE IN DISAGREEMENT

CLASSIFICATION OF PULMONARY DISEASE	PATIENTS WITH POSITIVE GASTRIC AND NEGATIVE TRACHEAL LAVAGE CULTURE FOR M. TUBERCULOSIS	PATIENTS WITH POSITIVE TRACHEAL AND NEGATIVE GASTRIC LAVAGE CULTURE FOR M. TUBERCULOSIS
Minimal	13	5
Moderately advanced	12	5
Far advanced	4	2

receiving the same chemotherapy but who had not had a tracheal lavage were also studied. In the first group, in only one case was there an increase in the amount of pulmonary involvement; all of the others revealed either no change or regression of the lesions. In the "control" group it was found that there was also one case of spread of tuberculosis. It is believed that the possibility of tracheal lavage leading to spread of pulmonary disease is very unlikely, particularly if the procedure is restricted to patients with sputum cultures negative far tubercle bacilli. A recent study was made of tuberculous patients who had undergone Lipiodol bronchography regarding the possibility that spread of pulmonary tuberculosis might be caused by the iodized oil (12). The writers concluded that such an occurrence was unlikely if the procedure was limited to the patient with controlled, stable, or regressive pulmonary tuberculous lesions.

DISCUSSION

While it is certainly true that it is often more difficult to pass a stomach tube than to perform a tracheal lavage, the latter procedure is more time-consuming. During the last six months of the present study, a record was kept of the time

required to do the two types of lavage. It was found that gastric lavage required an average of seven minutes, whereas a tracheal consumed twelve. When a satisfactory specimen could be obtained without topical anesthesia with Pontocaine, only five minutes were needed to do the tracheal; however, this was rarely possible. Such a time difference may be of little or no importance in private practice, but when many such procedures must be done each week it is an important consideration. While not occurring in the present series, the possibility that topical anesthesia might produce a systemic reaction must always be thought of, and the necessary drugs for combating such reactions should be immediately available.

The fact that a reliable and experienced technician can do the gastric lavage, whereas a physician should do the tracheal procedure, is also an important factor. Moreover, the physician should have experience in doing the tracheal lavage, even though it is a relatively simple and safe procedure. In a large hospital with a frequently changing resident and intern staff, it has been found that it is much more satisfactory to have gastric lavages performed than to instruct the individual members of the resident staff in the technique of the tracheal lavage (9). For the private physician dealing mainly with nonhospitalized persons, however, it is much more convenient to do a tracheal lavage. When the patient lives at a distance from the doctor, in order to do a gastric lavage, arrangements must be made for the patient to be at the laboratory early in the morning in a fasting state. Tracheal lavage may be done at the convenience of the patient and the physician.

The additional amount of equipment needed for the tracheal lavage should also be considered. To do a gastric lavage requires only a stomach tube and a syringe; to do a tracheal lavage requires Pontocaine, an atomizer, a special brush, a syringe, a tracheal cannula, sterile water, and a basin into which the patient can expectorate the Pontocaine. This too is relatively unimportant except when many tracheal lavages are being done.

It has been stated that the tracheal wash is well tolerated (5, 6). The experience of the present writers is in agreement with this statement; no patients have been encountered who refused to allow the procedure, and a suitable specimen for culture has always been obtained. During the period included in the present study it has been estimated by the technicians that, on approximately 8 occasions, either a patient has refused to allow a gastric lavage to be done or it has been impossible to do one. In spite of this, when 100 patients were asked regarding their preference, it was found that 56 chose gastric lavage, 34 tracheal, and 10 had no choice between the two procedures. Although not routinely asked, a number of patients volunteered the information that it was the unpleasant numbness and taste of the Pontocaine that influenced their decision.

It has been suggested that a patient can deceive a doctor with a gastric lavage (5). Eating or drinking water before the procedure can certainly negate its value. It would seem to be impossible to influence the results of the tracheal lavage in a comparable fashion. This is recognized as an argument in favor of the latter procedure.

That contamination of the atmosphere is much greater with the tracheal wash seems obvious, although no attempts were made to demonstrate this in the present study and no reports have been seen regarding it. For the average physician with limited office space available, this is an extremely important consideration. The operator may be well protected during the administration of the anesthesia and the lavage, but in obtaining a good specimen a cough must be elicited, and it is usually impossible for the patient to avoid spraying the surroundings with sputum droplets. There is no question that cough plates positive for tubercle bacilli can be obtained when held as far away as three feet from a patient with active pulmonary tuberculosis. The room in which the lavage is done should be considered potentially contaminated and should be meticulously cleaned after use.

SUMMARY

The writers believe that tracheal lavage as a method for obtaining specimens for the culture of *M. tuberculosis* is as good as, but no better than, the gastric lavage. The individual physician may prefer the tracheal lavage and may feel more confident in the results because he has done the procedure himself. Moreover, there are a number of factors unrelated to the relative "sensitivity" of the methods which must be considered before a choice between gastric and tracheal lavage can be made. As a test which must be done routinely on many persons each week, when evidence more certain than that revealed by culture of sputum negative for tubercle bacilli is desired, the gastric lavage is preferred by the present writers.

SUMARIO

Comparación de los Lavados Traqueal y Gástrico: Estudio de 463 Enfermos

Opinan los AA. que el lavado traqueal es un método para diagnosticar la tuberculosis pulmonar y determinar su actividad tan bueno como el lavado gástrico, pero no mejor que éste. Un médico dado puede preferir el lavado traqueal y abrigar más confianza en los resultados, por haber ejecutado el procedimiento él mismo. Sin embargo, antes de escoger entre el lavado gástrico y el traqueal, deben tomarse en cuenta los factores mencionados. Como prueba que hay que hacer rutinariamente en muchas personas cada semana cuando se desean datos más ciertos que los revelados por un cultivo "negativo" del esputo, los AA. prefieren el lavado gástrico.

RESUME

Une comparaison entre le lavage trachéal et le lavage gastrique: Etude de 463 cas

Les auteurs sont d'avis que le lavage trachéal comme méthode de diagnostic de la tuberculose pulmonaire et de la détermination de son activité est aussi bonne, mais non meilleure, que le lavage gastrique. Individuellement, le médecin peut préférer le lavage trachéal et se fier à ses resultats parce qu'il l'a effectué lui-même. Toutefois, les facteurs mentionnés ci-dessus doivent être pris en considération avant de faire un choix entre le lavage gastrique et le lavage trachéal. En tant que test devant être effectué de façon routinière chaque semaine sur un grand nombre de sujets et quand on desire obtenir une preuve plus sûre que celle fournie par une culture de crachats "négative," ces auteurs donnent la préférence au lavage gastrique.

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Editorial

The Relationship of the Immunity Mechanism to Pathologic Changes, Clinical Symptoms, and Therapeutic Measures in Tuberculosis[1]

In the treatment of tuberculosis one should take into consideration all of the complex pathologic conditions which are to be influenced by therapy. It has long been known that early, and even many advanced, lesions may heal as a result of the action of the patient's own natural and specific protective mechanisms. More recently measures have been added which are capable of greatly increasing therapeutic results, and it is necessary to understand in what manner they exert their favorable effects and also to know wherein they are deficient, because no perfect remedy has yet been found.

The pathologic conditions which present range from those found in mild lesions with fibrosis; acute lesions, with exudation, with or without destruction and cavity; to widespread chronic fibrosis, with or without exudation, caseation, and cavity. The prognosis differs with the extent and nature of the lesion, its location, and the reactive capacity of the patient.

In primary tuberculosis the body's reaction is similar to that toward any particulate matter. It is usually symptomless. But when infection has been once established and the individual's immunity mechanism awakened, the changes with which reinoculation is met are the result of the reaction between the bacilli and their products and the natural and awakened specific protective forces of the patient. This reaction is inflammatory and accompanied by symptoms.

Fifty years ago tuberculosis to most people meant certain death. To a few it meant life and suggested rest, eggs and milk, and living in the open air as measures necessary for its cure, because patients were regaining health under such treatment. The explanation for this was not known. Today, however, it is recognized that man's native resistance is best and his immune mechanisms most competent when his resistance is high.

In the years intervening since the early attempts at therapy, increased pathologic, bacteriologic, and immunologic knowledge have made it possible to understand the disease better. Nevertheless, there is a strong tendency to think of tuberculosis more in terms of therapeutic measures, such as hygienic living with rest and good food, compression, surgery, and antimicrobial drugs, than in terms of the fundamental reactions which should determine when and why these various therapeutic measures should be used.

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Fundamental to an understanding of the therapeutic problems is an appreciation of the manner in which the host protects himself and a recognition of the evidence of such protection.

[1] Presented in part before the Medical Session, as part of the symposium on the *Medical Aspects of Tuberculosis*, at the annual meeting of the National Tuberculosis Association, Los Angeles, California, May 18, 1953.

Clinical tuberculosis must be recognized as a struggle between the tubercle bacillus and the tissues of an immunized host. It may be described as a metastasizing, inflammatory, destructive, and curative process. The patient kills himself or cures himself according to the metastases which take place, the number and virulence of the bacilli which cause them, and the state of his resistance, natural and immunologic, at the time the metastases form or that he is able to develop in response to their stimulation. While the immunity reaction is the cause of destruction of tissues, at the same time it is the most important aid in the cure of the disease and one without which there would be no recovery.

We recognize the following as evidences of immunity which are met regularly in patients who suffer from clinical tuberculosis:

1. The entrance of bacilli into the tissues of the immunized host is antagonized, and their movement through the tissues is retarded.

2. Hundreds of millions of bacilli may be poured out into the air passages daily and pass over the bronchial mucous membranes of patients who suffer from destructive pulmonary disease without producing new metastases of clinical significance. The same is true of the intestines although large numbers of bacilli are swallowed daily. These facts should be sufficient to convince the most skeptical that the patient is endowed with strong protection.

3. Bacilli gain access to the blood stream frequently during the disease and may produce small foci in other organs such as the liver, kidney, spleen, bones, and joints, but rarely produce an advancing lesion.

These clinical experiences have many animal experiments, such as the following, upon which their explanation may be based.

Koch[2] observed that bacilli injected subcutaneously in a normal guinea pig ulcerate and remain ulcerated until the death of the animal, while bacilli injected in a pig which has been infected a few weeks previously also produce ulceration but go on to healing.

Webb and Williams[3] proved that the resisting power of animals could be increased specifically by injecting a single bacillus and then gradually increasing the number. In this manner animals were made to withstand 150,000 virulent bacilli without producing active disease.

Krause and Willis[4] showed that bacilli quickly pass from the primary focus to the regional lymph nodes in noninfected animals and make the circuit of the body in a few days; but in infected animals the passage is markedly retarded, requiring many days for the bacilli to reach distant organs.

Lurie[5] has shown that tubercle bacilli may live within leukocytes of a normal animal but die rapidly when the animal has been immunized by previous infection.

Manwaring and Bonfrenbrener[6] showed that 90 per cent of bacilli injected

[2] Koch, R.: Deutsche med. Wchnschr., 1891, *17*, 101.

[3] Webb, G., and Williams, W. W.: Tr. International Congress on Tuberculosis, Washington, D. C., 1908, vol. I, part 1, p. 174.

[4] Krause, A. K.: Am. Rev. Tuberc., 1924, *9*, 83.

[5] Lurie, M. B.: J. Exper. Med., 1942, *75*, 247.

[6] Manwaring, W. H., and Bonfrenbrener, J.: J. Exper. Med., 1913, *18*, 601.

intraperitoneally in guinea pigs previously infected were destroyed within one hour, while in a noninfected pig they produced infection.

Aside from the natural and specific protective powers of the body, mechanical changes take place which afford further aid in healing. An infiltrated lung contracts and becomes smaller; so does the bony cage; and the respiratory movement lessens. It readily may be seen that these changes are favorable to healing.

* * * * * *

Hygienic measures in the early years of treatment proved to be rational and successful sometimes in advanced cases. But advanced and destructive pathology with cavitation furnished special problems. Pneumothorax was introduced and was successful in many instances but still was not the perfect remedy hoped for. Pneumoperitoneum, thoracoplasty, and minor surgical measures were added. All of these compress the lung and lessen its movement, and so have become helpful measures.

Surgeons have now perfected their technique and offer aid in the way of resecting infected areas, cavities, lobes, and lungs, aid which was not thought possible but a short time ago.

Pneumothorax is now being displaced by pneumoperitoneum and surgery, partly because of the many failures and the complications which so often arise following its use. However, much of this injury may be avoided by using less pressure and stopping the refills when the desired result has been attained or when it has been reasonably determined that it will not be successful.

In advising surgery one must always bear in mind that there are many foci of infection in the lung outside the area which is chiefly involved. Such a thing as completely removing the infection is rare, and this fact must always be borne in mind. But patients may be prepared for the operation and be fairly well protected from activation afterwards by building up their physical strength and by the proper use of antimicrobial therapy.

Any form of treatment which reduces the functional capacity of the lung to any great extent must be considered carefully before it is employed. Patients who survive tuberculosis will often live for years, many to advanced age, and will now and then develop other respiratory diseases, such as pneumonia, acute or chronic bronchitis, bronchiectasis, asthma, emphysema, and a rigidity of the thorax. These make extra demands on the respiratory mechanism and, if its function has already been lowered by our therapeutic measures, the patient may be greatly incapacitated.

While chemotherapy has now come to the aid of the therapist, it is necessary to understand that it is an aid, not a cure. The chief function of our present antimicrobials is to prevent the multiplication of bacilli. Although one of our greatest therapeutic assets, it is not enough. We must still depend upon the patient's own protective forces—natural and acquired—for the destruction of the bacilli and healing of the lesion. Chemotherapy is of special value in preventing metastases from forming and, should they form, in checking their progression. It is in the acute types of the disease that it is most useful. Extensive, advanced, fibrotic lesions with destruction and cavity offer the greatest obstacles to its successful

action. This is also true of the patient's own natural and immunologic protective factors.

Jacobs and Kulms[7] have recently examined lungs removed by excision and shown that marked destruction and obliteration of the blood vessels take place. To overcome this effect they suggested that such remedies as the iodides and tuberculin be used. It has long been known that tuberculin produces a focal hyperemia. This makes it possible for the antitoxins, as well as the patient's own natural and immunologic protective substances, to come in more intimate contact with the bacilli in the tissues. In the treatment of tuberculous meningitis, tuberculin has been used intrathecally with reported advantage.

Bacilli sooner or later become resistant to antimicrobials but, by combining them, the time of the appearance of resistant strains may be postponed or prevented, and treatment may be carried on much longer than when they are used individually.

* * * * * *

There is no dependable cure in any single therapeutic measure for all of the many pathologic conditions met in the patient who suffers from advanced tuberculosis; but, if those we have are used understandingly, each for what it is capable of doing and properly reinforced by others, the treatment of tuberculosis may be remarkably successful. However, there has never been a time when it was more necessary than it is now to have accurate knowledge of the host, the disease, and the curative measures in order to treat patients intelligently and effectively. Research in the fundamentals of tuberculosis must go on. The better we understand the patient and his physiologic, bacteriologic, pathologic and immunologic reactions, the more successfully will the clinical problems be met.

It can be seen that anything which will improve the patient's resistance is indicated in all instances. While exudation and cavity will yield to the dietetic-open air-rest regimen, they can often be treated more successfully when collapse measures or surgery and antimicrobials are added. Antimicrobials have a special value in the presence of cavity because they act upon the disease in the bronchus, so favoring respiratory exchange and drainage.

No one who has been active in the treatment of tuberculosis during the past fifty years can fail to note the changes which have taken place in the clinical picture. The symptoms of the disease are less severe. Acute, so-called "galloping consumption" is now rarely met. Complications such as meningitis and tuberculosis of the larynx and intestines occur rarely, and the "good chronic" is a common rather than an occasional type. Resistance has lowered the susceptibility to infection, caused a decrease in the number of metastases in the infected, decreased the number of complications, and lowered the mortality rate. At the same time it has produced more chronics and prevented the morbidity rate from falling in proportion. This has been brought about, not by therapy alone, but also by the improved economic and social status of the people. Today, patients show more resistance to the disease and live longer with or without treatment.

[7] Jacobs, E. C., and Kulms, D. W.: Dis. of Chest, 1952, *22*, 523.

This is shown in the entire Western world as compared with the nations with a lower standard of living, where tuberculosis is still rampant in its acute forms.

If improved conditions in the economic and social status of the people will cause a reduction in the severity of the disease, reduce serious complications, increase the life span, and lower the death rate, this should be ample proof that the hygienic-dietetic-open air-rest regimen, which has for its purpose the making of the patient more resistant, is a true basis for therapy, no matter what other measures are used. In all instances the patient must cure himself.

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Notes

ANTAGONISM OF ISONIAZID BY CERTAIN METABOLITES

The high activity of isoniazid for mycobacteria indicates that the drug attacks the organism at some site vital to the cell's normal growth and multiplication. When cells are exposed to this drug, growth is not immediately arrested but continues until approximately one new generation has appeared. This bacteriostatic effect is independent of the concentration of isoniazid added and is of the type shown by the sulfonamide drugs. The mode of action of this latter group of drugs is linked with their ability to inhibit the synthesis of an essential metabolite, *p*-aminobenzoic acid. Because of the similarity of response demonstrated by susceptible organisms to isoniazid and to the sulfonamides, a survey was made of a wide variety of substances in an attempt to find a growth factor or metabolite which would neutralize the inhibitory effect of isoniazid on the growth of tubercle bacilli.

Growth experiments on the virulent H37Rv strain of *M. tuberculosis* were conducted in a Tween 80[1] medium without albumin in calibrated test tubes, and optical density readings were taken on a Coleman Junior spectrophotometer throughout a fourteen-day incubation period. Compounds tested included 21 of the naturally occurring amino acids, the B-complex vitamins, and known intermediates of the Krebs cycle.

Of the compounds tested, antagonism of isoniazid was obtained only with α-ketoglutarate, sodium pyruvate, pyridoxal,[2] and pyridoxamine. Pyridoxal was more effective than the keto-acids in interfering with isoniazid activity. A relationship was observed between the drug concentration and the concentration of the vitamin required. In cultures which had been completely inhibited for fourteen days by incubation in the presence of 0.05 γ of isoniazid per ml., growth could be initiated by the addition of 10 γ of pyridoxal hydrochloride per ml.

Respiration studies have also been made on virulent H37Rv tubercle bacilli using standard Warburg techniques. Isoniazid was found to inhibit the endogenous respiration of these organisms as well as the oxidation of a number of typical substrates (glucose, glycerol, pyruvate, lactate, acetate). The inhibitory effect of isoniazid on the endogenous respiration was completely neutralized when pyridoxal, pyridoxamine, or α-ketoglutarate was added to the Warburg vessel. Antagonism of isoniazid by these compounds was complete after five hours of incubation with the drug, at which time the oxygen uptake had reached the control level.

On the basis of these findings, it is apparent that isoniazid interferes with some phase of the metabolism of tubercle bacilli involving pyridoxal. The similarity in chemical structure between isoniazid and pyridoxal suggests a true antagonism of the competitive type between isoniazid and this essential metabolite. The ability of α-ketoglutarate to neutralize the inhibitory action of isoniazid is believed to be due, not simply to the chemical interaction of the keto group with the hydrazine group of isoniazid, but to be linked with essential metabolic reactions in which pyridoxal is known to function as the coenzyme

[1] Tween 80 is the proprietary name for the polyoxyethylene derivative of Sorbitan monooleate, obtainable from the Atlas Powder Co., Wilmington, Delaware.

[2] Metabolically active form of pyridoxine.

and α-ketoglutarate as one of the essential reactants. Studies are now in progress to investigate this hypothesis further.

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September 15, 1953

Correspondence

TREATMENT OF TUBERCULOUS LYMPHADENITIS WITH SODIUM SALICYLATE

To the Editor of The American Review of Tuberculosis:

I am fully aware that the following report is far from complete. Nevertheless, I wish to pass on the idea for further investigation under more favorable conditions than those prevailing in Hongkong.

Recent publications on tuberculosis show that, to achieve the progress made in chemotherapy, thousands of chemical compounds had to be tested for their bacteriostatic qualities (Barry, V. C.: The Royal Institute of Chemistry, Lectures, Monographs and Reports, 1952, No. 2). Domagk alone tested "several thousands" for the Bayer works (Domagk, G.: Beitr. z. Klin. Tuberk., 1948, *101*, 365). Their choice of compounds was made empirically rather than from chemical considerations. The most effective antituberculous drugs so far known are chemically very diverse. They have, however, one feature in common: they all have one basic nitrogenous group in their chemical constitution (derivatives of diaminodiphenyl sulfone, thiosemicarbazones, *p*-aminosalicylic acid, isoniazid, anilinoaposafranin, and long-chained hydroxy-amines). It is assumed, therefore, that some connection exists between the basic nitrogenous group and a compound's bacteriostatic qualities.

During the last twenty-five years I have been using sodium salicylate against tuberculous lymphadenitis with remarkable success. Since sodium salicylate does not possess a basic nitrogenous group and its chemical structure is relatively simple, compared with the other effective drugs, my experience with it might be of interest to the experimental biochemist and clinician alike. No animal experiments preceded the introduction of this drug. This should, however, not detract from the value of my observations, since the last word on the efficacy of a drug rests with the clinician.

My attention was called twenty-five years ago to sodium salicylate as an antituberculous drug by a Dutch doctor from Java whose name I have, unfortunately, forgotten. After convincing myself of the efficacy of this treatment, I applied it in several hundred cases of lymphatic tuberculosis by intravenous or intramuscular injections, with satisfactory results. I do not recollect one single case in which I had to resort to operation or X-ray treatment. Since the introduction of para-aminosalicylic acid as an antituberculous drug, I took up treatment of tuberculous lymphadenitis with sodium salicylate on a larger scale. The results were satisfactory, as before.

Seventy-five patients were treated in this series; they were 90 per cent Chinese of all age groups under twenty. The Chinese were of the lowest social class, underfed, and living under the most primitive housing conditions. Only those patients were accepted for treatment whose chief sign was tuberculosis of the lymph nodes. Bone and pulmonary cases were not included in this series, although mild lung infections could not always be excluded. The cases were all advanced, with lymph nodes more than walnut size, often with sinuses and tuberculous ulcers. A similar group of cases was treated by methods other than sodium salicylate (PAS, streptomycin) and used as controls. The diagnosis was purely clinical and was not confirmed bacteriologically; nevertheless, there was little doubt about its correctness.

Children up to six years of age were given 1 to 2 cc. of 10 per cent sodium salicylate intravenously two to three times a week. Older children and adults received 5 to 10 cc.

in increasing doses. If the veins were too small, intramuscular injections were given. No other drugs were administered during the sodium salicylate treatment.

The recording was made by a diagram: a large V represented the medial edges of the sternomastoid muscle, and the glands were marked with their size and number in relation to the muscle. The size was described as egg-, plum-, walnut-sized, et cetera. The change was marked every two to four weeks.

With the exception of 5 cases in which the generalized tuberculosis developed, all of the lymph node lesions responded to treatment. The nodes decreased in size and disappeared gradually within three to nine months, according to their original size and the general condition of the patient. The response was often dramatic, and was noticed after the first five to ten injections. Large nodes became soft in the center and had to be aspirated. Occasional sinuses and ulcers healed with further treatment. The core of the nodes did not always disappear completely; a hard fibrous center was then palpable. The treatment had no ill effect on any of our patients. On the contrary, their general condition improved rapidly and they gained in weight in spite of their poor feeding and housing conditions.

Those treated with sodium salicylate compared very favorably with the controls treated with PAS or streptomycin. When a general infection was manifest, the sodium salicylate treatment was combined with streptomycin. Such cases are not included in this report. The impression was gained, however, that the two drugs had an integrating effect on each other.

Sodium salicylate has the advantage over other drugs in that it is relatively nontoxic and apparently no drug-fast bacilli are produced by the treatment. It is effective in smaller doses than PAS or streptomycin; sometimes even one injection a week had a favorable effect. No difference was noticed between the effect of the intravenous and intramuscular administration. The impression was gained in a few cases that sodium salicylate given by mouth has not the same effect as when given parenterally. This should, however, be tried on a larger scale.

No attempt was made so far to treat tuberculosis other than tuberculosis of the lymph nodes. Should other workers confirm my favorable results, the extension of salicylate treatment to other forms of tuberculosis would be a logical step. Animal and culture experiments would also be of interest. Since such experiments did not precede my clinical work, no opinion can be expressed on the action mechanism of sodium salicylate. This problem is further complicated by the possibility that sodium salicylate acts on the lymphatic system and not on the bacteria.

Should it be found, however, that sodium salicylate has a bacteriostatic action on tubercle bacilli, this fact may well be an indication to the experimental chemist which group of the complicated compounds now in use is the essential factor.

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January 12, 1953

ESTABLISHMENT OF A BERYLLIUM CASE REGISTRY

To the Editor of the American Review of Tuberculosis:

A man-made illness of considerable interest has been reported in the medical literature in this country since 1943 under various titles, in general referring to its association with

exposure to certain beryllium compounds. As the years go by, more cases continue to appear from a variety of industrial and research operations using beryllium compounds. With funds supplied by the Atomic Energy Commission, it is planned to develop a beryllium case registry at the Massachusetts General Hospital. The purpose is to enable a study of the epidemiology of this disease, an evaluation of the beryllium hazard of incriminated operations, and dissemination of knowledge of the clinical course of beryllium poisoning, especially relative to its medical management. The material collected is to be available for study, and from time to time data will be sent to participating physicians summarizing facts which have been established.

This description is being published in the hope that physicians, roentgenologists, and pathologists who have knowledge of cases of beryllium poisoning will wish to participate in making this beryllium case registry complete. We have facilities and funds for prompt handling of any material which is submitted such as case records, X-rays, and tissue. It is planned to keep cases which are entered in the registry anonymous.

We shall welcome any correspondence.

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Yours very truly,
HARRIET L. HARDY

August 19, 1953

Books

TREATMENT OF RESPIRATORY EMERGENCIES INCLUDING BULBAR POLIOMYELITIS. By Thomas C. Galloway. Pp. 94, Charles C Thomas, Springfield, Illinois, 1953, Price, $3.00.

This, I believe, is an extremely important contribution to the medical literature on a subject of interest to all clinicians. Dr. Galloway has not implied that we have yet advanced to an exact and scientific state in analyzing respiratory emergencies. Rather, he has astutely compiled his personal experience and impressions along with the few available facts to present an excellent guide to the care of such cases.

One cannot emphasize too strongly some of the well-chosen points made in this monograph. In our experience, the great need is for *early* tracheotomy in the case of bulbar poliomyelitis, even at the expense of doing a few unnecessarily. As an internist, I can only agree with Dr. Galloway that teamwork among physicians caring for these people is of the essence. Each step toward placing a patient in a respirator should be explained to the conscious patient, as well as to the inexperienced resident staff. In this manner, much of the patient's fear is allayed and he is better able to cooperate. As pointed out by the author, a clear airway—with or without tracheotomy—must be assured before the artificial respiration is begun.

A point not within the scope of this book, but one which has provided considerable difficulty in our experience, is the one of finding the proper level of artificial respirations. The settings (15 to 20 respirations per minute and negative 15 cm. of water pressure) outlined by Dr. Galloway may or may not result in hypocapnia. If this does in fact represent a state of hyperventilation for the patient, the problems of electrolyte balance and ultimately of weaning become important also. Outside of arterial pCO_2 levels, there is as yet no adequate, simple manner of evaluation in this situation.

The matter of postural drainage in the cases under question, and also in chronic pulmonary disease, has long been neglected by clinicians. This is especially so since the advent of antimicrobial drugs, which we know are many-pronged weapons and under whose blanket we cannot hide all of our ignorance. Man, in his upright state of existence, might better in some instances be stood on his head, for only in this manner can the mechanical problem of bronchial drainage be overcome. The English, I believe, are ahead of us on this score, as postural drainage is a routine in such cases as warrant it.

Finally, I should like to urge all clinicians to avail themselves of Dr. Galloway's work, for there is a message for all specialists as well as the general practitioner in this monograph. The author is to be applauded for his simplicity of style and honesty of presentation.

JOHN A. KING
Geneva, New York

THE BACTERIOSTATIC ACTIVITY OF 3500 ORGANIC COMPOUNDS FOR MYCOBACTERIUM TUBERCULOSIS VAR. HOMINIS. By Guy P. Youmans, Leonard Doub, and Anne S. Youmans. Pp. 713, The National Research Council, Washington, D. C., 1953, Price, $5.00.

In this publication of the Chemical-Biological Coordination Center of the National Research Council, the authors present the results of the *in vitro* testing of the bacteriostatic activity of 3,500 synthetic organic compounds against virulent human tubercle bacilli

and *in vivo* tests of 184 compounds for their suppressive action against tuberculous infection in mice.

As a preface to the listings of the activities of the compounds both *in vitro* and *in vivo*, Dr. Youmans devotes a chapter to the explanation of the rationale covering the use of the tests employed for potential therapeutic activity and an additional chapter to the detailed description of the methods used in performing these *in vitro* and *in vivo* tests. A very interesting section is concerned with the discussion of the relation of chemical structure to bacteriostatic activity within certain chemical series of compounds.

As the authors point out, although the results of the tests of this large number of compounds are essentially negative from the standpoint of discovering a suitable chemotherapeutic agent for the treatment of tuberculosis, they are, however, significant in that their documentation can prevent the unnecessary labor of duplication of effort in other laboratories working on the same problem. Much information of a positive nature can also be gleaned from this volume which may have considerable importance from the academic standpoint, such as the section on the relation of chemical structure to bacteriostatic activity.

That this publication, which for the most part consists of documenting the chemical structure and test results of this large series of compounds, will be of value and interest to the investigator engaged in evaluating agents having potential antituberculous effect is a tribute to the clear, well-organized method of presentation by the authors.

ROBERT M. MCCUNE
New York, New York

SECTIONAL RADIOGRAPHY OF THE CHEST. By Irving J. Kane. Pp. 154, with illustrations, Springer Publishing Co., Inc., New York, 1953, Price, $7.50.

Following an interesting foreword by Dr. Edward D. Churchill, the author presents the historical background, terminology, underlying principles, and technique of planigraphy of the chest. Next are sections on the normal anatomy and pathology followed by diagrams and reproductions of roentgenograms.

The section devoted to technique is particularly good. Outstanding is the discussion of radiation hazard with attention directed to the fact that the danger is negligible providing reasonable care is employed.

The author wisely stresses the fact that planigraphy should be practiced in a thorough fashion. He thinks that restriction of the initial study to certain levels or portions of one hemithorax as well as omission of the lateral views may well be false economy.

The diagrams are clear, and the reproduction of the films is excellent. The films were carefully selected to demonstrate technique, normal anatomy, pathology, and the advantages of sectional radiography over conventional film studies alone. The separation of the diagrams and film reproductions from the explanatory text is awkward.

A complete bibliography is included, and the index appears workable.

There are few good tests on body section radiography. This book is one of them and is recommended to those studying or employing this modality.

FORBES DELANY
Greenwich, Connecticut

BOOKS RECEIVED

A PRACTICE OF THORACIC SURGERY. By A. L. d'Abreu. Pp. 591, with illustrations, Williams & Wilkins Company, Baltimore, 1953, Price, $14.50.

ASPECTS OF THE PSYCHOLOGY OF THE TUBERCULOUS. By Gordon F. Derner. Pp. 119, Paul B. Hoeber, Inc., New York, 1953, Price, $3.50.

IMMUNITY, HYPERSENSITIVITY, AND SEROLOGY. By Sidney Raffel. Pp. 531, Appleton-Century-Crofts, Inc., New York, 1953, Price, $8.00.

THORACIC SURGERY AND RELATED PATHOLOGY. By Gustaf E. Lindskog and Averill A. Liebow. Pp. 644, with illustrations, Appleton-Century-Crofts, Inc., New York, 1953, Price, $5.00.

NUTRITIONAL STUDIES IN ADOLESCENT GIRLS. And Their Relation to Tuberculosis. By Joseph A. Johnston. Pp. 330, with illustrations, Charles C Thomas, Springfield, Illinois, 1953, Price, $7.50.

DISORDERS OF THE CIRCULATORY SYSTEM. By the New York Academy of Medicine. Pp. 305, The Macmillan Company, New York, 1952, Price, $5.50.

BAKTERIOLOGISCHE NÄHRBÖDEN. By Lothar Hallmann. Pp. 252, Georg Thieme Verlag, Stuttgart, 1953.

EXTRAPULMONALE TUBERKULOSE. By A. Wernli-Haessig. Pp. 154, S. Karger, Basel and New York, 1952, Price, 14.60 Swiss francs.

EL PLOMBAJE CON MATERIAL PLASTICO EN LA COLAPSOTERAPIA QUIRURGICA DE LA TUBERCULOSIS PULMONAR. By Fernando Alberto Medici. Pp. 118, Libreria y Editorial "El Ateneo", Buenos Aires, 1952.

SCHOOLS OF PUBLIC HEALTH IN THE UNITED STATES. By Leonard S. Rosenfeld, Marjorie Gooch, and Oscar H. Levine. Pp. 110, Public Health Service, U. S. Department of Health, Education, and Welfare, Washington 25, D. C., 1953, Price, 35 cents.

American Trudeau Society

Medical Section of the National Tuberculosis Association

Report of the Committee on Therapy to the Committee on Medical Research, May 16, 1953

The Committee held two meetings during the year. The first was held in New York on October 7 and 8, 1952, and copies of the report presented to the Committee on Medical Research at its meeting on October 9 were distributed with the minutes.

The second meeting of the Committee was held at the Biltmore Hotel, Los Angeles, California, on May 16, 1953. Members present were: Dr. Robert H. Ebert, Chairman, Col. Carl W. Tempel, Dr. David T. Carr, Dr. Karl H. Pfuetze, and Dr. William B. Tucker. Committee members not present were: Cmdr. Charles A. Castle, Dr. John Maxwell Chamberlain, Dr. Nicholas D. D'Esopo, and Dr. John B. O'Connor.

Guests present were: Dr. John D. Steele, Secretary-Treasurer, American Trudeau Society, and Miss Agnes Fahy, Associate in Public Relations, National Tuberculosis Association.

The following topics were discussed:

Toxicity of Isoniazid and Iproniazid

Dr. David Carr presented a statement on the toxicity of isoniazid and iproniazid. After some minor revisions the report was accepted with thanks and it was recommended that it be published in THE AMERICAN REVIEW OF TUBERCULOSIS.

Tuberculous Meningitis

Therapeutic failures still occur in at least half of the adult patients with tuberculous meningitis. A physician treating the occasional case of meningitis is sometimes at a loss to know the best method of treating the disease. For this reason the Committee on Therapy asked Col. Tempel to prepare a statement on the treatment of tuberculous meningitis. Col. Tempel presented a preliminary draft and the Committee expressed the opinion that the report was excellent and made only a few minor changes. It was decided that the report should also include the treatment of tuberculous meningitis in children, and Col. Tempel was asked to prepare such a statement with the collaboration of Dr. Edith Lincoln of Bellevue Hospital. It was suggested by the Committee that when the report is completed it be submitted to THE AMERICAN REVIEW OF TUBERCULOSIS for publication.

Report of the Subcommittee on Retrospective Studies

The final report of the Subcommittee on Retrospective Studies was read and was accepted with a few minor changes. The subcommittee made the following recommendations:

1. That the Committee on Revision of Diagnostic Standards of the American Trudeau Society give consideration to devising a much more nearly complete method for the classification of pulmonary tuberculosis, stressing *extent*, *location*, *age*, and *character* of disease. If such a method can be devised, and put into general use, differences in methods of reporting data and possibly differences in results of treatment from different clinics may be reduced materially.

2. That the Committee on Revision of Diagnostic Standards give consideration to including in the next issue of *Diagnostic Standards* an outline of the basic principles of good statistical analysis of data.

3. That the American Trudeau Society or its Committee on Therapy keep a file

of the correspondence and unpublished manuscripts of the Subcommittee for the future use of interested parties, and offer consultation service to individuals or institutions interested in making retrospective studies of the treatment of pulmonary tuberculosis.

4. That the American Trudeau Society do not attempt to sponsor cooperative retrospective studies of the therapy of pulmonary tuberculosis.

5. That the Subcommittee on Retrospective Studies be discharged.

A motion was passed that the report be accepted with a vote of appreciation.

Functions of the Committee on Therapy

This item was discussed at a luncheon meeting. Those present included members of the Committee on Therapy and, among others, Dr. David A. Cooper, Dr. Floyd M. Feldmann, Dr. Daniel E. Jenkins, Dr. Esmond R. Long, Dr. Carl Muschenheim, Dr. Donald J. Ottenberg, Dr. James E. Perkins, and Dr. John D. Steele.

The purpose of the luncheon was to discuss the activities and the functions of the Committee on Therapy. It was the consensus that the Committee should analyze recent data even though they are incomplete and should attempt interpretation even on controversial matters. It was emphasized that such statements were opinions based on available data and not necessarily final judgments. It was believed that statements should reflect the opinion of the Committee on Therapy and need not be approved in detail by the Council.

Formation of a Committee on Pulmonary Function

The Committee discussed the wisdom of setting up a committee on pulmonary function. Dr. Tucker expressed the opinion that the field of respiratory physiology is in a period of rapid growth, is developing new techniques, and includes the study of many pulmonary conditions in an attempt to delineate the nature of the impairment of function in various diseases. He suggested that there was relatively little cohesiveness among many of the investigators in this field and thought there was a real place for a group of experts to get together and define areas of agreement or those suitable for further common study. A motion was passed that the Committee go on record as favoring the formation of such a committee on pulmonary function by the Council.

Joint Meeting with the Laboratory Subcommittee

A joint meeting was held with the Laboratory Subcommittee and there was vigorous discussion on the importance of isoniazid-resistant organisms which are apparently avirulent for the guinea pig. It was emphasized in the discussion that no evidence was available to suggest that these organisms were avirulent for humans.

Respectfully submitted,

David T. Carr
Charles A. Castle
John Maxwell Chamberlain
Nicholas D. D'Esopo
John B. O'Connor
Karl H. Pfuetze
Carl W. Tempel
William B. Tucker

Robert H. Ebert, *Chairman*
Committee on Therapy

Report of the Committee on Therapy for Its Subcommittee for Retrospective Studies, May 16, 1953[1]

The need for comprehensive data on the results, both early and late, of different forms of treatment of pulmonary tuberculosis was recently re-emphasized by the Clinical Subcommittee of the Committee on Medical Research, now the Committee on Therapy of the American Trudeau Society.[2] Acting on this recommendation, a Subcommittee was created to explore the practicality of a cooperative study of this kind from as wide a variety of sources as possible. Emphasis was placed not so much on obtaining a definitive analysis of the effects of different variables on the outcome of such treatment as on lessening the differences in reporting of results from different sections of the country.

The Subcommittee has met on five occasions in the two years of its existence and one interim report has been published.[3] At the first meeting, ways and means of planning a country-wide retrospective study sponsored and possibly financially supported by the American Trudeau Society were discussed. By the third meeting it was agreed that such an ideal goal was wholly impractical. Efforts were directed instead toward writing "The Adaptation of Hospital Records to Current and Retrospective Studies of the Therapy of Pulmonary Tuberculosis." By the time a third draft entitled "A Guide to the Retrospective Study of the Therapy of Pulmonary Tuberculosis" had been prepared and the fifth meeting had been held, it was clear that even this more practical approach to the problem was unsatisfactory, for the following reasons:

1. No method of record keeping could be made suitable for studies of past discharges as well as for future studies of current admissions.

2. The most valuable retrospective studies are designed to meet a limited or specific objective and are apt to go into too much detail to be included in a standardized form suitable for general use.

3. The rapid changes in both the major features and minor details of the treatment of pulmonary tuberculosis may make plans for possible future studies relatively meaningless.

4. The diminishing use of some measures, e.g., phrenic nerve operations, pneumothorax, conventional thoracoplasty, has reduced the need for retrospective studies of results observed with them.

5. The various controlled studies of chemotherapeutic regimens now in progress (Medical Research Council, Veterans Administration, Public Health Service) and the Veterans Administration plans for controlled studies of resection, pneumoperitoneum, and rest therapy during prolonged chemotherapy reduce the need for retrospective studies of these subjects.

The greatest difficulty in planning satisfactory retrospective (or prospective controlled) studies of the treatment of pulmonary tuberculosis is the lack of satisfactory and uniform methods of classifying the *extent*, *location*, *age*, and *character* of disease. There can be no doubt that differences in results from different clinics or different parts of the country are frequently explained by gross differences in these background factors. The

[1] H. H. Fellows, 1951–1952; Shirley Ferebee, 1951–1953; Julia Jones, 1952–1953; Hiram Langston, 1951–1952; Roger S. Mitchell, *Chairman*, 1951–1953; Rufus Payne, 1951–1953; William S. Schwartz, 1951–1953; Norman J. Wilson, 1952–1953.

[2] Reports of the Clinical and Laboratory Subcommittees, American Trudeau Society, Am. Rev. Tuberc., 1951, *63*, 496.

[3] Report of the Subcommittee on Retrospective Studies on Therapy, Am. Rev. Tuberc., 1952, *66*, 643.

variations of extent in the present classification of *minimal*, *moderately advanced*, and *far advanced* are too great. It has also been shown, for instance, that the prognosis of very early disease is quite unpredictable; furthermore, chronic fibroid disease has a pattern of response to all presently available methods of treatment quite different from that of the average more recent case of tuberculosis. Most important, the character of disease (the amount of reversible pneumonia compared with the amount of necrosis) has a profound effect on results of treatment. The effect of location of disease on various forms of treatment is in need of clarification.

Experience with retrospective studies has shown them to be full of pitfalls for the unwary. In particular, when seemingly two parallel series of patients treated at different points in time are compared, there may be many important differences, such as the frequency of taking routine films, methods of treatment, the attitudes of different physicians toward various clinical manifestations, and even the behavior of tuberculosis in general.

Failure to take into account the timing of relapse or death, and differences in starting point of observation, differences in duration of observation, and differences in the fact and condition of survival may introduce gross error into retrospective observations. This error can, however, be minimized by the use of the life-table principle of analyzing data. The changing health status, duration of relapse, and recurrence of relapse should also form a part of the picture. The Subcommittee strongly recommends the use of the life-table principle in reporting all studies in which length of survival, timing of relapse, changing health status, and similar factors are concerned. Other less complex but equally important statistical principles frequently are overlooked in the collection and presentation of data.

Retrospective studies in essence serve to document *what* has happened without always clearly defining *why*. On the other hand, many important advances in our knowledge of clinical medicine have come from what has amounted to the retrospective analysis of the personal experience of a careful observer.

In concluding its deliberations over a two-year period, the Subcommittee makes the following recommendations:

1. That the Committee on Diagnostic Standards of the American Trudeau Society give consideration to devising a much more nearly complete method for the classification of pulmonary tuberculosis, stressing *extent*, *location*, *age*, and *character* of disease.[4] If such a method can be devised, and put into general

[4] Example of the method recommended:
"*2-2FA; old, 2 yrs. +; M ⅔ resolv., 5C; RU 3C H; RM, LM: L; LU .5C M; RL, LL: O.*"
The meaning of this formula would be as follows:
a) *2-2FA:* means moderately advanced in each lung, far advanced combining the two.
b) *Old, 2 yrs.:* means estimated age of majority of disease is "old," i.e., more than 5 years; new = 2 years or less; medium 2 to 5 years. Two years plus means *available* films *show* disease for at least two years.
c) *M ⅔ resolv., 5C:* means over-all character of shadows is "medium" (4 degrees in all = "light", (*L*); "medium" (*M*); "heavy" (*H*); and "unknown" (*?*)). About two-fifths of shadows appear "resolvable," i.e., three-fifths appear to represent irreversible necrosis; and total diameter of all cavities (*C*) in both lungs is 5 cm.
d) *RU, RM, RL, LU, LM, LL* = 6 divisions (not lobes) of lung or lung fields, with *LM*, for instance, representing left mid-lung field.
e) *3C and .5C* diameter (in cm.) of *largest* cavity (*C*) in section.
f) *O* means no visible disease.

use, differences in methods of reporting data and possibly differences in results of treatment from different clinics may be reduced materially.

2. That the Committee on Diagnostic Standards give consideration to including in the next issue of *Diagnostic Standards* an outline of the basic principles of good statistical analysis of data.

3. That the American Trudeau Society or its Committee on Therapy keep a file of the correspondence and unpublished manuscripts of the Subcommittee for the future use of interested parties, and offer consultation service to persons or institutions interested in making retrospective studies of the treatment of pulmonary tuberculosis.

4. That the American Trudeau Society do not attempt to sponsor cooperative retrospective studies of the therapy of pulmonary tuberculosis.

5. That the Subcommittee for Retrospective Studies be discharged.

Signed:

Members of the Committee on Therapy

DAVID T. CARR
C A. CASTLE
J. MAXWELL CHAMBERLAIN
NICHOLAS D. D'ESOPO
JOHN B. O'CONNOR
KARL H. PFUETZE
CARL W. TEMPEL
WILLIAM B. TUCKER

ROBERT H. EBERT, *Chairman*

Report of the Laboratory Subcommittee to the Committee on Medical Research, May 16, 1953

The Laboratory Subcommittee held two meetings during the year. The first meeting was held in New York on October 7, 1952. Copies of the report of that meeting, which was presented to the Committee on Medical Research on October 9, 1952, were distributed with the minutes of the meeting of the parent committee.

The second meeting was held in Los Angeles on May 16, 1953. At both the fall and spring meetings, a portion of the time was spent in joint session with the American Trudeau Society Committee on Therapy. A report of the deliberations at the May meeting follows.

1. Drug resistance and virulence of tubercle bacilli isolated from patients before, during and after chemotherapy with isoniazid alone and in combination with other drugs: The overwhelming majority of tubercle bacilli isolated before the initiation of chemotherapy with isoniazid from the sputa of human beings suffering from pulmonary tuberculosis are sensitive to less than 0.5 γ of isoniazid per ml. of culture medium. Similarly, in accord with the past experience of many investigators, strains of tubercle bacilli isolated from the sputum of human beings before chemotherapy almost invariably possess significantly high virulence for the guinea pig.

It has recently been observed by several investigators that, during chemotherapy with isoniazid, striking changes take place in the properties of populations of tubercle bacilli isolated from patients: Increasing proportions of isoniazid-resistant tubercle bacilli appear in the sputa of patients whose sputa remain positive; and remarkable decreases occur in the guinea pig virulence[1] of parts or all of the populations recovered from sputa of some patients during treatment with this agent. Indeed, not only have these organisms been observed to be different from isoniazid-sensitive parent strains of tubercle bacilli with respect to isoniazid-sensitivity and often with respect to virulence, but they are often different with respect to their growth requirements on artificial media.

The Subcommittee wishes to emphasize that, in spite of the experimental work indicating that some strains of tubercle bacilli highly resistant to isoniazid *in vitro* are nonpathogenic for guinea pigs under certain experimental conditions, *there is no evidence that these strains are nonpathogenic for human beings.* In point of fact, progressive tuberculosis has been observed to occur in patients whose sputa consist predominantly of tubercle bacilli which are highly resistant to isoniazid *in vitro* and are nonpathogenic for guinea pigs. In the light of these facts, there is at present no basis for altering the established methods of control of active pulmonary tuberculosis (by chemotherapy, et

[1] In order to avoid confusion concerning the meanings of certain terms used in this report, the Subcommittee has seen fit to define the words "pathogenicity" and "virulence" as follows, with full realization that definitions are arbitrary and that these definitions may not be generally acceptable: (*1*) a microorganism is said to be pathogenic when it is capable of causing disease by multiplication in any host; it may be pathogenic for one species of host and nonpathogenic for another; (*2*) virulence refers to the degree of pathogenicity of a particular strain of microorganism for a specific host under a specific set of experimental conditions; in particular, the term is used when comparing strains of pathogenic microorganisms which are very similar and, indeed, may be considered so closely related as to be classified as mutants.

cetera) because of the laboratory observations as to the diminished virulence associated in some cases with isoniazid resistance.

There are not sufficient bacteriologic studies available at present to permit any statements concerning what happens to the bacterial populations in closed or open lesions in patients after interruption of therapy with isoniazid.

Finally, the Subcommittee feels justified in concluding from the presently available data that the administration of isoniazid in combination with streptomycin and/or PAS to patients whose sputa contain a large proportion of tubercle bacilli sensitive to these latter agents delays somewhat the appearance of variants of those organisms resistant to these drugs. Furthermore, several studies suggest that on prolonged therapy the conversion rate (positive to negative for tubercle bacilli on both smear and culture) is higher in such patients than in similar patients treated with isoniazid alone.

2. The Subcommittee has been asked by several investigators to formulate a statement on the present state of knowledge of the viability of tubercle bacilli in closed necrotic lesions. It was evident that the question was raised in the hope that an authoritative opinion could be expressed which would be of assistance to clinicians who might use it as a guide in cases in which excisional surgery or similar treatment was under consideration. The Subcommittee thought it would be unwise at this time to attempt such a formulation, because (*1*) the significance of the term "viability" has not yet been defined to the full satisfaction of all concerned, and (*2*) there is not yet sufficient agreement among investigators on the basic facts pertaining to the problem of growth and pathogenic properties of tubercle bacilli in residual lesions to permit the construction of an acceptable statement.

This Subcommittee does recommend, however, that bacteriologists, pathologists, and surgeons collaborate more intensively in the study of pulmonary lesions removed surgically from patients with pulmonary tuberculosis. There is no rational basis for incompatibility between these groups. Specifically, it is suggested that the following methods be adhered to in the handling of such specimens:

(*1*) The specimen is sent in a sterile container to the bacteriology department (so that the specimen inadvertently may not be fixed). From this point on, handling of the specimen should be under the guidance of the bacteriologist. It is believed that a clinician familiar with the patient from whom the specimen is obtained should be present during these procedures.

(*2*) In the main, three types of lesions should be carefully studied: the open cavity, the closed cavity, and necrotic foci which have not sloughed.

(*3*) Each lesion should be incised separately with sterile instruments. The wall of the lesion and the necrotic center should be separately removed and each placed in sterile containers. They should be individually handled for culture and animal inoculations. This separation is feasible only with large foci, particularly in the case of inspissated cavities. In other instances the entire lesion must be handled as a single unit, but both the wall and the necrotic center should be included in the specimen for culture.

(*4*) Smears should be made on slides before cultures are made, and without contamination of the specimen.

(*5*) Until further information is available, the methods of culture of such materials are left to the discretion of the bacteriologist. However, animal inoculation as well as culture of artificial media are recommended wherever possible.

(*6*) The specimen is then returned to the pathologist, who is primarily interested in the gross and microscopic appearance of the cavity wall, the adjoining bron-

chus, and the tissue surrounding the lesion which is studied by the bacteriologist. When an entire nonsloughed area is given to the bacteriologist, other similar lesions should be studied by the pathologist.

Respectfully submitted,

Oscar Auerbach
Wendell H. Hall
Gladys L. Hobby
John R. McDonald
Emanuel Wolinsky

Gardner Middlebrook, *Chairman*
Laboratory Subcommittee

Why Give Pneumoperitoneum or Pneumothorax?

Report of Panel Discussion Held at the Annual Meeting of the American Trudeau Society, Los Angeles, California, on May 19, 1953

Moderator—William B. Tucker, Minneapolis, Minnesota
Members of Panel: Nicholas D. D'Esopo, West Haven, Conn.
Giles Filley, Trudeau, New York
Gordon M. Meade, Trudeau, New York
Julius L. Wilson, Philadelphia, Pa.
Norman J. Wilson, Brookline, Mass.

Dr. Tucker: We will declare this session opened. This is one of the two last sessions of the medical program of this annual meeting of the National Tuberculosis Association. The other one is looking forward, "The Future of the Bacteriology of Tubercle Bacilli with Isoniazid Therapy." This one has a flavor of looking backward; but perhaps there is some merit or advantage in looking back to help us with the future. And so with that let me start out and ask Nick D'Esopo the first question. What is a pneumothorax supposed to do?

Dr. D'Esopo: With pneumothorax I think it's prime two purposes are: one, to close cavities; and the other, to control progressive disease.

Dr. Tucker: You think then that the pulmonary cavity is one of the main lesions which is the objective of pneumothorax therapy? Is that right?

Dr. D'Esopo: Pulmonary cavity and the metastases from the pulmonary cavity, yes.

Dr. Tucker: Would you agree with that, Julius?

Dr. Julius Wilson: Yes, I should think the cavity and all that goes with it, such as rapid conversion of the sputum and bronchogenic spread. I don't like the word "metastases."

Dr. Tucker: Anyone else on the panel care to comment on that? No? O.K. We're going to go to pneumoperitoneum and ask Gordon Meade—What's pneumoperitoneum supposed to do?

Dr. Meade: Well, I would say that the purposes of pneumoperitoneum were to achieve essentially the same results as a pneumothorax, only in a different way.

Dr. Tucker: What different way?

Dr. Meade: Simply that you do not collapse the lung proper. You have elevation of the diaphragm, restriction of motion, without actual lung collapse.

Dr. Tucker: Do you think it is the same kind of lesion which is affected favorably by pneumoperitoneum as by pneumothorax, Gordon?

Dr. Meade: I would think so.

Dr. Tucker: Any opposite or alternate point of view? Dr. Norman Wilson?

Dr. Norman Wilson: Yes, I'd like to take a little exception to that. I've never felt that pneumoperitoneum was nearly as effective as a pneumothorax for stemming the progress of an active lesion. I'm not against giving pneumoperitoneum (I don't want to be misunderstood) but it never seemed to me that they were just quite similar.

Dr. Tucker: Gordon?

Dr. Meade: I think we are agreed really, Norman, on that. It wasn't a question of relative effectiveness; it was a question of what they were applied for.

Dr. Norman Wilson: May I ask a question? Have you ever used pneumoperitoneum to stop progression of disease—active exudative disease?

DR. TUCKER: That's a good leading question, Gordon.

DR. MEADE: Yes, I think we have cases where pneumothorax is not possible.

DR. TUCKER: There are certain physiologic considerations in this and I'm going to ask Giles Filley. Without being too technical, Giles, what in a general way are the physiologic effects of a pneumothorax?

DR. FILLEY: Well, in contrast to pneumoperitoneum, pneumothorax provides a much more selective collapse and, if one believes that the effectiveness of therapy is proportional to the amount of collapse, then there is good physiologic support for Dr. Norman Wilson's opinion that pneumothorax should be more effective on physiologic grounds. However, it is, or was before the advent of chemotherapy, distinctly more hazardous, primarily because of the increased danger of complications.

DR. TUCKER: We are going to come back to this question of pneumothorax and chemotherapy just a little later. First, we are trying to get some of the fundamental principles. Do you believe that there is importance in the degree of effective collapse in the control of the infection, Giles?

DR. FILLEY: That primarily is a clinical question. On physiologic grounds there is likelihood that pneumothorax should be more effective. I think a lot depends on whether you believe that interference with lung motion is more important than interference with lung distention. Pneumoperitoneum does not interfere with lung motion inasmuch as the vital capacity is hardly affected at all. The main thing pneumoperitoneum does is reduce the volume of the lung at the end of a quiet expiration by about 30 per cent. The lung is less distended but you can still take a deep breath with pneumoperitoneum. The lung under a pneumothorax can never expand nearly to the same extent as the other.

DR. TUCKER: That's a beautifully clear statement, Giles. You have anticipated my next question, so I'm going to turn to Julius Wilson and ask him—Do you think the degree of collapse in pneumothorax is important?

DR. JULIUS WILSON: The degree of collapse of the actual lesion in the lung is, of course, important and unless one secures so-called selective collapse of the diseased area and closure of cavity by blocking the bronchus or actual approximation of the walls, the treatment naturally is a failure. However, that does not mean complete collapse of the lung and it means very little subtraction from the vital capacity. In treating moderately advanced and minimal lesions, the vital capacity is no more affected than it would be with a good pneumoperitoneum.

DR. TUCKER: We're still getting background now. I'll ask Gordon Meade—How often in 100 pneumothoraces undertaken with the proper indications is it possible to establish satisfactory collapse?

DR. MEADE: Of course, that depends entirely on what criteria you establish for satisfactory collapse and end results. I think that in our group of cases analyzed at Trudeau, some 550 cases, a satisfactory collapse initially was obtained in less than 50 per cent. You don't want me to go into a definition of what we consider a satisfactory collapse?

DR. TUCKER: No. We know what has come out of Trudeau on this and we can refer to those papers and get those figures. I recall in Max Pinner's book, *Pulmonary Tuberculosis in the Adult*, he analyzed, say, 100 hypothetical cases, and came down to less than 15 per cent which could actually in the run of the mill cases of tuberculosis carry on with satisfactory pneumothorax. Of course that was a number of years ago. What do you think, Gordon, about the possible place for pneumonolysis in helping to get a satisfactory pneumothorax?

DR. MEADE: I think it's extremely important because in the cases which we studied we found that there was a very close relationship between the effectiveness of the result

at one year and three years after abandonment with respect to whether or not adhesions had been present. Now, it made little difference whether or not the collapse was obtained spontaneously or as a result of lysis. The important thing was to be free of adhesions one way or another.

DR. TUCKER: I know that there are many minor questions but that is a broad general statement which I think would meet with general approval.

DR. NORMAN WILSON: I'd like to take a little issue with that. I've always, even before the days of drugs, considered cutting adhesions one of the most radical thoracic operations we've ever had. And as far as I'm concerned, if you do any extensive cutting of adhesions, especially if you abide by some of the things in the literature (such as going out and peeling out the extrapleural space as advocated by some), the incidence of bleeding in the pleural space and fixation of lungs, unexpandable lungs, empyemas, have a sharp rise in incidence. And I'd like to throw back a question to Dr. Meade. I agree with him that, as far as the patient's disease is concerned, cutting adhesions and getting a free pneumothorax is important but you have entered into a realm of immeasurable complications which hardly anyone could anticipate. And, therefore, from the standpoint of the patient's disease, I think probably oftentimes we did more harm than good.

DR. TUCKER: I'm sure Gordon agrees largely but I'm going to let him speak again on that.

DR. MEADE: Well, again, we certainly are in agreement because the statement that I made that the good results were directly related to the absence of adhesions does not mean by any means that I advocate that they always be cut. I think one has to evaluate very carefully the suggestion in each particular case and then make up his mind whether it is safe and proper to do a lysis. If you can't, then I think it is better to abandon the pneumothorax.

DR. TUCKER: I think most physicians would agree with both Dr. Wilson and Dr. Meade on that. This question of complications of pneumothorax is of course one of the most important aspects of this evaluation of this contribution to the control of pulmonary tuberculosis. I want to ask Julie what is his impression as to how frequent the complication rate of pneumothorax is? In rough terms, is it high, medium, or low?

DR. JULIUS WILSON: Of course, the principal trouble with treating tuberculosis with pneumothorax is that the lesions are subpleural and it is almost impossible to avoid some soiling of the pleura; so, when we put 50 to 60 per cent of our patients under pneumothorax treatment, the rate of collection of fluid was well over 50 per cent. That included all stages and types of disease. On the other hand, if you collapse minimal tuberculosis with "positive gastric" or "positive sputum" without definite cavitation, your rate of effusions falls way down somewhere around 10 to 15 per cent, properly handled. We have never had the privilege of handling enough cases of pneumothorax under proper protection of antibiotic therapy to know what we could do with that. For instance, the surgeons now operate doing segmental resections, lobectomies. How many would like to go back to doing this without the protection of the antibiotics? And yet those are the conditions under which we used pneumothorax fifteen years ago;—right up to two or three years ago, as a matter of fact. So it was asking a good deal not to have the pleura actually infected. The major thing is that only about 5 per cent of these patients ever had really serious difficulties with empyema.

DR. TUCKER: Anyone challenge that 5 per cent figure? Gordon?

DR. MEADE: In our particular series in which there were very few minimals (they were mostly moderately and far advanced), the rate of empyema (of course one runs into a definition of empyema here) was 18 per cent. And the very disturbing thing, carrying that further, was that the mortality rate among that 18 per cent was 43 per cent.

DR. TUCKER: Julie, even though as you say we didn't have the opportunity to use pneumothorax in the modern chemotherapy era, what would you think, judging by the nature of the complications of pneumothorax, as to the effect the availability of chemotherapy might have upon the complication rate?

DR. JULIUS WILSON: I have no way of knowing that, of course; but it would seem to me that, if you have a disease which is potentially a progressive fatal disease and you have three different treatments consisting of bed rest, chemotherapy, and collapse therapy, all working more or less in different ways, you should at least give the patient the benefit of all three types of treatment until you know better. Also, I would like to point out that we never really learned to use pneumothorax properly and to get out of there when it was dangerous to persist until just before the treatment began to lose its popularity entirely. It was pointed out by Rafferty and others along about 1945 that, if you had adhesions and they weren't cutable string adhesions, you had better get out of there at once.

DR. NORMAN WILSON: I realize that Julie was referring to infectious complications and assume that for the time being you are excluding crippling loss of function as a complication?

DR. TUCKER: I think he was speaking primarily along that line, yes; but I would, of course, include that.

DR. NORMAN WILSON: I would like to throw out a question then to the panel. Is there anyone here who feels that he can define the potential loss of function even in a minimal lesion when he introduces a pneumothorax? Can he estimate where it is going to fall even with a reasonable degree of accuracy?

DR. TUCKER: Giles, you're the expert on that.

DR. FILLEY: Well, with a reasonable degree of accuracy, one can predict that, if the pneumothorax in a minimal lesion is not associated with any fluid formation, there will be no measurable loss of function. If there is fluid formation, you can get any degree of loss of function as an end result, from zero to a totally nonfunctioning lung.

DR. NORMAN WILSON: Is that regardless of the duration of the pneumothorax?

DR. FILLEY: I wish I could answer that question.

DR. NORMAN WILSON: That is very pertinent because most of them were from three to five years.

DR. FILLEY: That's right. There is no clear-cut evidence that the length of time in which a lung is collapsed is in itself necessarily followed by failure of that lung to perform properly when re-expanded. The problem is, however, that, in general, the longer a lung is down, the more chance there is for pleural thickening and fibrosis to occur.

DR. JULIUS WILSON: I'd like to ask Norm a question. Can he predict before removing an upper lobe how much the loss of function is going to be?

DR. NORMAN WILSON: I can't, but Dr. Gaensler can. He's studied lots of them and I go to him and he tells me it is pretty measurable and very definite.

DR. JULIUS WILSON: Even when the case is complicated?

DR. NORMAN WILSON: Well, we know how many cases are going to be complicated.

DR. JULIUS WILSON: Well, we know with pneumothorax too.

DR. TUCKER: Yes, the question is certainly one of variability. I would think that the variability of loss of function would be greater with pneumothorax than with resection.

DR. NORMAN WILSON: That's what I was driving at. Max Pinner years ago pointed out that, of all the procedures we use, the unpredictable loss of function falls into the category of pneumothorax patients.

DR. TUCKER: Gordon, you want to say something?

DR. MEADE: I would agree with Dr. Filley, too, that the loss of function is related

to the duration of the pneumothorax; but we also have some figures that perhaps go along with that; namely, we tried to estimate the degree of contraction of lungs following pneumothorax and found a very definite relationship between the degree of contraction and the duration of pneumothorax. When the pneumothorax was only of six to twelve months' duration, there was little or no contraction in about 70 per cent of the patients. When the pneumothorax was up to three to six years, there was marked contraction in over 25 to 45 per cent.

DR. TUCKER: I thought that Giles as a physiologist was a pretty good clinician when he pointed out that it wasn't the duration of pneumothorax per se which results in loss of function but that longer duration leads to more pleural inflammatory lesions. You're really saying the same thing.

Nick, is there any figure you care to give as the probable complication rate with pneumoperitoneum? How frequent are significant complications of pneumoperitoneum? Fairly frequent, not so frequent, rare, what would you say?

DR. D'ESOPO: I understand they're quite rare, but I don't think I'd care to give a figure, Bill.

DR. TUCKER: Gordon?

DR. MEADE: I can't give you any figures but I would agree with Nick that they are rare.

DR. TUCKER: You both agree that they are considerably less frequent than with pneumothorax. Julie?

DR. JULIUS WILSON: I would certainly agree that they are considerably less frequent than with pneumothorax, but I think they are very commonly overlooked and ignored. Certainly about 10 per cent of the cases are complicated by some irritation of the peritoneum and various degrees of fluid, but when you open the thorax or you roentgenograph the thorax you don't see the fluid in the abdominal cavity; whereas with pneumothorax you are able to see as little as 10 to 15 cc. of fluid in the pleural space.

DR. TUCKER: Do you think, Julie, that, if we had chemotherapy available when we were using pneumoperitoneum, in some parts of the country more extensively than at present or in the experience of others as far as you know, that using chemotherapy reduces the frequency of any complications?

DR. JULIUS WILSON: I have no figures to substantiate that, but that is my distinct impression, that complications are less frequent in patients taking antibiotics simultaneously.

DR. TUCKER: I'll ask Giles another question. Is partial loss of function of one lung that you referred to as the result of pneumothorax too big a price to pay for the effect of pneumothorax—that it might contribute to recovery?

DR. FILLEY: Before the days of chemotherapy it often was too big a price to pay because tuberculosis is a disease which tends to be life-long and may involve the other lung. Although you may arrest the disease in one lung at the expense of its function, the other lung would frequently become involved and definitive therapeutic procedures, particularly surgical, were difficult to carry out inasmuch as the first lung was not functioning However, many things may change in this regard because of the advent of chemotherapy.

DR. TUCKER: Would it not also depend on the availability of alternative procedures?

DR. FILLEY: Very much so.

DR. TUCKER: Another question, Giles. Is not some thickening of the pleura possibly of some protection against reactivation of tuberculosis?

DR. FILLEY: I can't answer that from any physiological data we have. If you believe that interference with lung motion is a help in the healing process, I would say yes.

DR. TUCKER: Gordon?

DR. MEADE: I don't believe we have any evidence from our study to give us any answer to that.

DR. JULIUS WILSON: There is a curious thing in the statistics on relapse after prolonged pneumothorax. In the French statistics and in a series which I analyzed, reactivation occurs about five times as frequently in the opposite lung in those cases which have had a satisfactory collapse for as long as three years. That would seem to indicate two things to me: One, that this isn't just a problem of metastasizing from a caseous necrotic focus because these patients all had long-term "negative" sputum; and, two, that the thickening of the pleura which does occur over the collapsed lung, particularly over the part that's diseased, has a certain protective action against relapse.

DR. NORMAN WILSON: May I ask a question? Do you think the fixation interferes with bronchial cleansing? If a patient did have a little infectious sputum, he might get into more trouble than if he didn't have the fixed lung?

DR. JULIUS WILSON: I don't know that. I wouldn't worry about bronchial cleansing as long as the bronchial tree was intact, and the mucosa was intact.

DR. TUCKER: That sounds like one of those things we don't know too much about. I'll turn to another question to Julie Wilson. What location of a cavity in a lung do you feel is most likely to respond to an artificial pneumothorax?

DR. JULIUS WILSON: Well, of course, tuberculosis in all parts of the lung responds to pneumothorax and it is possible to obtain selective collapse of the lower lobe and segments and middle lobe when they're free. However, the fact remains that patients with tuberculosis in the central and lower portions of their lungs are, by and large, individuals less resistant to tuberculosis and poorer risks; also such lesions have poorer drainage and give rise to many more complications in the bronchial tree.

DR. TUCKER: Gordon?

DR. MEADE: Well I'd like to disagree somewhat with that. It appears to us that it makes little difference in the final result as to whether the cavity is located in the apex, the infraclavicular region, or base, provided one has free collapse.

DR. TUCKER: Gordon, while you have the microphone, what is your impression as to the location of a tuberculous lesion which responds best to pneumoperitoneum therapy?

DR. MEADE: Well, it would be distinctly an impression only. But we have the impression that those which respond best are probably in the apex of the lower lobe.

DR. TUCKER: I am going to go rapidly on to another question, Gordon. After abandonment of a satisfactory pneumothorax, what is the relapse rate?

DR. MEADE: If one takes all those cases which at the time of abandonment could be considered a good result, then follows those for periods of up to eighteen years, one finds that the reactivation rate at the end of eighteen years is in the neighborhood of 22 per cent. The great majority of those reactivations come within the first three years (15 per cent).

DR. TUCKER: It varies, I presume, with the extent of the disease at the start.

DR. MEADE: Yes.

DR. TUCKER: Do you have either data or impressions, Gordon, of reactivations after the abandonment of pneumoperitoneum?

DR. MEADE: No. I do not have any figures which would compare to those on pneumothorax.

DR. TUCKER: Is it your impression that it is higher or lower than after pneumothorax?

DR. MEADE: I think our impression at the present time is that it is possibly lower.

DR. TUCKER: Does anyone else have any impressions? Nick? Julie? I'm afraid that our own material has not been studied so thoroughly as the series on pneumothorax, although

it is my impression that the relapse rate after pneumoperitoneum is fairly high and may be as high as that reported by the Trudeau group for pneumothorax. But from any of these data or from clinical experience, is there any indication, Gordon, in your analysis as to the optimal duration of pneumothorax?

DR. MEADE: We divided the cases into those who had anywhere from six months to three years of pneumothorax, and then those who had more than three years and, much to our surprise, we found no difference in the two groups in the long-term results.

DR. TUCKER: Norm Wilson, do you have results on duration of pneumothorax?

DR. NORMAN WILSON: Well, of course, we are looking back now. We all feel differently now about pneumothorax. Do you want me to answer that looking back or for the present.

DR. TUCKER: Looking back, first.

DR. NORMAN WILSON: Yes, I think that if a pneumothorax has not healed a lesion in three years, it ought to be abandoned in favor of something else. If you can't expand the lung safely in that time, then you can never expand the lung safely in the majority of instances.

DR. TUCKER: What about less than three years, Norm?

DR. NORMAN WILSON: In most instances I think three years is too long. But I think going back again to the concepts we had in the pre-chemotherapy days,—and that's pretty hard to go back to and be fair in your judgment—I was one who felt that if pneumothorax was started and was successful it should be kept up two to three years. And that was probably an error in judgment as we look back. At the time I think that was in keeping with what most of us thought was good practice.

DR. TUCKER: It certainly was with me too, Norm. Again it was the lack of availability of other procedures at that time. We were getting along all right so we stayed with it for a while.

DR. JULIUS WILSON: I'd like to put in at this point a little disagreement there. I think the collected figures from other series, from France, have shown that the relapse rate was greater in the cases treated less than three years; and after three years there was no great increase. That was our experience in West Haven too. I should also like to say something about the matter of time alone. At a panel similar to this at Atlantic City, the chief objection raised to pneumoperitoneum and pneumothorax was the fact that the patient was a slave to the needle for three years. It seems to me that is of the essence of the problem aside from the physiologic factors about which we don't know. But the success of pneumotherapy, if you want to call it that, depends on the fact that the patient sticks with the doctor for three years or more and does what the doctor says. I don't think we can throw that out entirely. It sounds like a mystic, rather than a scientific, fact; but, whatever the treatment used, I still think it is an important factor. The patients who stayed over three years had a much lower relapse rate in my experience and in the literature.

DR. TUCKER: You could say the same thing about pneumoperitoneum, Julie.

DR. JULIUS WILSON: Absolutely; I think some of the series of pneumoperitoneum cases that have been presented, such as Dr. Trimble's here in Oakland and other series, have been successful largely on the same basis that they were series of cases in which the failures dropped out early and the cooperative well-disciplined patient stuck to the doctor faithfully through five years and got an excellent result.

DR. TUCKER: You have some reaction?

DR. D'ESOPO: Well, I'd like to speculate a moment about duration of pneumothorax. I think, now that we have some data on the bacteriology of closed lesions, it is interesting to wonder if a patient who received a pneumothorax and finally got well didn't remain

well because it took the bacilli that long to die in these closed lesions. I think looking at the X-ray during the course of the pneumothorax it was impossible to tell how long it would take for these organisms to die off. At Sunmount, Dr. Medlar had the opportunity to study some lesions that had been under pneumothorax for a while. We got these specimens because the patient had a decortication and a resection. He found that these necrotic lesions still had a potential bronchial communication, so that morphologically there would be no reason why these things should heal. I think there is a question now whether the lesions that healed under pneumothorax may not have healed for bacteriologic rather than morphologic reasons. I think in that light it might be understandable why patients who had pneumothorax for five years may have done better than those who had it for two years.

DR. JULIUS WILSON: I want to ask you about this potential bronchial communication. Are these somewhat similar to a valve which is turned off and kept turned off? Four or five years?

DR. D'ESOPO: Well I don't know about the valve, but I'll describe what it really was. Dr. Medlar found that the bronchi were still potentially open. They were filled with necrotic material and he could insert a fine wire probe from the bronchus into the filled-in cavity.

DR. JULIUS WILSON: What I'm trying to get at is, isn't it possible that the success of pneumothorax is due to the fact that we can very promptly shut off the opening to the cavity and convert the sputum and maintain that condition by skilled balancing of tensions or collapse, or whatever you want to call it, long enough so that the bacteriological process which has been rediscovered under chemotherapy can take place?

DR. D'ESOPO: That's what I said.

DR. JULIUS WILSON: What I'm trying to get at is that this potential open cavity can be kept closed when you have the patient on pneumothorax, but it can't if you turn your patient loose after nine months of bed rest.

DR. D'ESOPO: The idea was that when the pneumothorax was re-expanded you still had a necrotic lesion with an open cavity and you still had this open bronchus. The patient remained well because the lesion was sterile.

DR. TUCKER: I want to ask Giles Filley what happens to the diaphragm after three years of pneumoperitoneum? Does it return to perfectly normal function?

DR. FILLEY: Yes, sir. There is no change in diaphragmatic function.

DR. TUCKER: What happens if phrenic crush is added?

DR. FILLEY: Well, phrenic crush itself is moderately effective in reducing pulmonary function. As a rule, these phrenic paralyses have been temporary. However, there is a distinct impression since phrenic crush and pneumoperitoneum have been combined that the exceedingly high elevation of the diaphragm seen when the phrenic nerve is crushed in the presence of pneumoperitoneum is followed by a higher incidence of permanent paralysis than without the pneumoperitoneum.

DR. TUCKER: Norman, do you think there is a place for phrenic in the treatment of pulmonary tuberculosis today?

DR. NORMAN WILSON: Personally, I don't; and I never do one unless the medical man takes responsibility for it.

DR. TUCKER: I want to come now very briefly to the question of ambulatory pneumothorax. Julie, do you think there is a place for ambulatory pneumothorax? What was your impression when it was used and studied in a few places?

DR. JULIUS WILSON: We have been talking lately about ambulatory chemotherapy in patients. The first thing we have to do is define the term ambulatory. If by that you mean

the treatment can be continued after the patient is up and out of bed in the hospital, after he has been discharged from the hospital and is home and being rehabilitated, I would say that is one of the great strengths of pneumotherapy.

DR. TUCKER: How about initially, right from the start?

DR. JULIUS WILSON: No. I'll hold no brief for such treatment. I think the big experiment carried out in Chicago is one of the best answers to that. Anyone who is interested should study the reports of the Chicago experiment.

DR. TUCKER: Julie, what about ambulatory pneumoperitoneum? Not after a period of hospitalization, but all the way through?

DR. JULIUS WILSON: I feel the same way about it although the immediate hazard will be less. I think it is a very poor and unsatisfactory substitute for hospital treatment.

DR. TUCKER: Giles, from a physiologic standpoint, is there any basis for advising against ambulatory pneumoperitoneum?

DR. FILLEY: Well, on the contrary, from a physiologic standpoint you can get the same amount of collapse with a pneumoperitoneum on an ambulatory basis as you do when you put the patient to bed and give him no specific external form of collapse. The reason for this is that bed rest is in itself a form of collapse in as much as the functional residual capacity when one lies down is 30 per cent reduced. When the patient stands up and receives pneumoperitoneum, the functional residual capacity is again reduced 30 per cent. If you really believe that reduction of lung tension is a form of collapse which aids the healing of tuberculosis, then there is a physiologic basis for the ambulatory treatment by pneumoperitoneum.

DR. MEADE: I'd like to ask Dr. Filley what happens when you give a patient a pneumoperitoneum and you also put him to bed?

DR. FILLEY: Then you get about 40 per cent collapse.

DR. NORMAN WILSON: I'd like to ask what happens when he stops standing and starts walking? Your test no longer holds; is that not true?

DR. FILLEY: So far as the functional residual capacity is concerned, it still is true. That's been measured during exercise and it is the same as it is in standing. We actually have not made the test of exercise with pneumoperitoneum but I would predict that it is the same. However, you are entirely right with regard to another part of this collapse business. During exercise you do take deeper breaths and pneumoperitoneum won't stop you from doing that.

DR. TUCKER: Well, I think that has been a very helpful contribution from Giles. Gordon, is there any evidence that pneumoperitoneum improves the results of good, long, combined streptomycin-PAS chemotherapy?

DR. MEADE: Well, we have some very preliminary figures which indicate that, when the cavities are three centimeters or more in diameter, the combination of pneumoperitoneum and chemotherapy, namely, streptomycin and PAS, is better than chemotherapy alone in achieving cavity closing and sputum conversion.

DR. TUCKER: Is that difference great?

DR. MEADE: No, but possibly significant.

DR. TUCKER: But there is a question in that, it seems to me. If we give combined pneumoperitoneum and chemotherapy simultaneously, how can one determine that pneumoperitoneum makes a contribution to the over-all result?

DR. MEADE: We attempted to compare apparently comparable cases, those who were on chemotherapy and those who were on chemotherapy in combination with pneumoperitoneum, and to rate the speed of cavity closure and the speed of sputum conversion.

DR. D'ESOPO: But you selected the cases for pneumoperitoneum, they weren't selected by chance; there is some reason why you gave the pneumoperitoneum.

DR. MEADE: That is correct. That is why I say the figures are possibly open to question.

DR. TUCKER: Well, certainly, this question should be susceptible to an answer, and I think there is a plan on foot in certain institutions to study very critically the effect of pneumoperitoneum along with chemotherapy by carefully controlled studies. So I think, in answer to my own question, it is certainly possible to get the data and I think in the next year or two we will have some. Nick, do you believe that what has generally been credited to pneumothorax or pneumoperitoneum in the past could be achieved equally well with good chemotherapy alone?

DR. D'ESOPO: I consider the two real contributions of pneumothorax the closure of cavity and the halting of progressive disease. For the latter indication, chemotherapy is of course excellent. That is really its greatest usefulness. That immediately relieves us of one of the benefits of pneumothorax, that is the halting of progressive disease. As for cavity closure, we at Sunmount have purposely avoided collapse therapy only to learn the effectiveness of certain regimens on cavity closure. That's the thing that's still unfinished. We have the general impression that, when cavities are four centimeters or less in diameter, the great majority do close with effective original chemotherapy, with certain variations in the position of the cavity. I rather think that larger cavities, larger than four centimeters, might be helped by adjunctive collapse therapy, but I certainly don't know that.

DR. TUCKER: Well, that's quite an admission from Nick D'Esopo in case you didn't know it. So I am going to ask him another one. With good combined chemotherapy and in an original case, that is, the ideal one for such treatment, do you think a good reversible collapse procedure without complications would help what could be achieved by that chemotherapy alone? Possibly getting there faster if not more certainly?

DR. D'ESOPO: I think, if you gave half of such cases chemotherapy alone and you gave the other half pneumotherapy also, those who got the pneumotherapy would win out. That doesn't mean that these two procedures are better. It means that there are certain cases. Our real problem is to try to select from the mass of material those cases which require adjunctive collapse therapy. I am now talking on the premise that our basic therapy is chemotherapy, and in some cases you need something other than chemotherapy.

DR. TUCKER: Fair enough, and I'm going to ask you another question, related. If we used pneumotherapy in a more widespread fashion along with our chemotherapy, do you think that that would reduce the amount of bed rest that would be needed or would it shorten the hospital stay?

DR. D'ESOPO: I suppose it would, but I think the important thing now is how to pose a question. What I mean by that is that, if you know how to ask the question, you are well on your way to the solution of it. I think we shouldn't try to guess at this stage of the game. We should really try to ask the right questions. The question you asked me is the question we are asking our patients, really. I don't want to answer it.

DR. NORMAN WILSON: Could I ask a question here because to me it is one of the things I need help in and I think it is very important. These questions to me have assumed that we are making decisions at the very beginning, which not many of us do in treating tuberculosis. When we put a patient on drug therapy we might want to wait three months to see how he is doing before making a decision. I'd like to ask Nick, from his vast experience with chemotherapy, if he had a fairly good case, let's say a patient who had a five-centimeter cavity, who was put on chemotherapy and at the end of four months still had

a three-centimeter cavity which had been stationary for two months, what would he then do?

DR. D'ESOPO: Well, if the cavity is still open at the fourth month and shows no tendency to close, we do one of two things: apply pneumo-therapy in an attempt to close the cavity, or that cavity might be collapsed surgically or resected. Now in a case such as you describe, very often the patient goes through a phase of negative cultures. Even though the cavity is still open, the cultures are negative for several months. I think it might be preferable to resect that open cavity during that negative culture phase rather than to apply pneumo-therapy. Now, there are cases we can't resect. Either the patient is a poor risk or there are bilateral cavities or something like that, and in those cases I think pneumo-therapy should be applied. I think, if by the fourth month the cavity shows no real trend towards closure, that one should think of adjunctive therapy, pneumo-therapy, thoracoplasty, or resection.

DR. TUCKER: You see this question of resection inevitably got dragged in, even though it's not in the title. Actually we've got to consider it and we'll come back to it, but we still have some other things to take up first. Julie, with good chemotherapy, do you feel the disadvantages outweigh the advantages of pneumothorax?

DR. JULIUS WILSON: I don't see how you can answer that for all cases. You have to answer it for each individual involved. I can still see the medical student with his recently discovered infraclavicular lesion in his senior year in medical school facing the possibility of a year of bed rest, resection, and another year of bed rest; whereas the same individual with a pneumothorax might lose a month or so and go on to finish his medical school and go on to internship, which is perfectly possible. Many of them have done it.

DR. D'ESOPO: I thought you didn't believe in ambulatory pneumothorax.

DR. TUCKER: Well, I'm going to let that one ride. I think Julie made a very positive statement there. Maybe he can do that in Philadelphia where he told me the other day that they have a fourteen-month backlog on beds, or something like that. But what I really had in mind was that, I think, in general, pneumothorax has been abandoned because the disadvantages outweighed the advantages. That was really before we had good chemotherapy. I just wondered whether with chemotherapy in general, not in a few specific instances, you felt that it still outweighed the advantages.

DR. JULIUS WILSON: No, I meant to imply that under the proper indications there is still a narrow field for pneumothorax. That is my opinion.

DR. TUCKER: Now, I'll come right back at you again. We concentrate on one person at a time, you see. What about pneumoperitoneum? There seems to have been a decline in its use in various parts of the country in recent years, perhaps because of the availability of other procedures. Do you think its disadvantages or its potential disadvantages outweigh its advantages? I think your answer will be different here than for pneumothorax.

DR. JULIUS WILSON: I don't know why you think the answer will be different. You mean it can just be thrown at anybody? I think it is a safer procedure but I think we have many staff meetings where the staff gives up its choice of any individual treatment.

DR. TUCKER: Gordon, sort of a summarizing question on this. Was it the use or abuse of pneumothorax which led to its damnation just when chemotherapy might have made it safe?

DR. MEADE: I wouldn't really say abuse. I think it was the fact that we had not learned to properly select cases that led us to begin to realize that the results that we were getting over a prolonged period were not satisfactory and not what we had hoped.

But I think that recently, at just about the time chemotherapy was coming in, we began to analyze results and get a much clearer idea of what were the satisfactory indications.

DR. TUCKER: I think that's very true. Norm, I'm going to come to thoracoplasty and talk about the thoracoplasty type of operation and ask you not to be too specific on what you insist about extrapereosteal plombage and so on, and ask you how you rate a thoracoplasty type of operation with pneumothorax in essentially the same kind of a case?

DR. NORMAN WILSON: You'll have to define the case for me. Are you speaking of an exudative lesion?

DR. TUCKER: No; subacute; cavernous, unilobar, upper lobe tuberculosis.

DR. NORMAN WILSON: In my estimation there's never been a comparison. When you do a thoracoplasty on a patient he usually converts, he is discharged from the institution with medical consent with a lasting cure that is second to nothing we have ever had, including resection.

DR. TUCKER: You feel that it has a greater initial success?

DR. NORMAN WILSON: Very much so. It is applicable in the first place to a much larger group of the tuberculous population, and your failures in the past with thoracoplasty also have now been defined. In other words, if you go back five years you'll find out that we were doing thoracoplasty in cases which everyone today accepts as an indication for resection. Therefore, if we become more intelligent in using thoracoplasty as we go along, our initial successes should be greater. (I don't like to get mixed up with initial successes and failures and the late-term results of successful thoracoplasty cases; they are two entirely different things.)

DR. TUCKER: Well, I was just trying to break it down, Norm. I was wondering how you compared the thoracoplasty type of operation with pneumothorax initially, in regard to complications, and then the late results.

DR. NORMAN WILSON: Well, initially it is applicable to many more people, with many more kinds of disease and to people who can't receive pneumothorax because of adherence, for instance; I think the initial success is very much higher and the lasting cures in my estimation can't be compared.

DR. TUCKER: Giles, from a physiologic standpoint, what is the impairment of a thoracoplasty, either the standard three-stage or the extrapleural or periosteal?

DR. FILLEY: Well compared to pneumothorax I would say that, in general, the loss of function is less so long as your thoracoplasty is confined as much as possible to the diseased area. We've got some very remarkable results in preservation of function when the thoracoplasty has been carried out whereby virtually only diseased tissue is collapsed. You end up with a better functional result by far than you do with a complicated pneumothorax.

DR. NORMAN WILSON: May I ask some questions to supplement this? Dr. Filley, is it not true that, if a thoracoplasty is done (the chief reason we do thoracoplasty is for the same indication as for resection of the apical posterior segment of the lung), if we do not violate the principle that you and Dr. Wright and others have laid down and don't go around on the third rib to the cartilage, if we do a selective thoracoplasty and stay above the sixth rib and preserve the anterior portion of the third rib, would you not agree that the loss of function is minimal?

DR. FILLEY: I agree entirely. I think the third rib is a very important rib to think about.

DR. TUCKER: There's another question about thoracoplasty which I think many of us have tended to overlook. It is generally agreed, I think, that the initial conversion rate of

thoracoplasty is in the neighborhood of 70 per cent. That can be improved, of course, by secondary procedures. But one of the great strengths and merits of thoracoplasty has been its low relapse rate. Well, Nick, directing the question to you, here is a relatively low relapse rate after a successful thoracoplasty. Is there any indication of the nonviability of the acid-fast organisms?

Dr. D'Esopo: It might be, but I think we have to consider how the patient came to thoracoplasty. A thoracoplasty patient is a very highly selected person. He has been able to keep his large areas of necrosis in one lung. He has stabilized those lesions, and I think he is selected as a person who has shown acquired immunity and, therefore, becomes a candidate for thoracoplasty. I think that is one feature. The other is that it seems that thoracoplasty patients have a low relapse rate even though their cultures are positive frequently. I think it gets down to the size of the sloughing lesion. Some of these thoracoplasty patients have slit-like cavities. The sloughing area is really quite small. Because of that, they may remain well.

Dr. Tucker: You can certainly see the reason for my asking you. Here is a treatment, an irreversible surgical procedure which has rather generally come to be accepted as having a low relapse rate and not involving resection. Is there any information why this procedure has had that low relapse rate and yet the relapse rate after pneumothorax and possibly pneumoperitoneum has been higher?

Dr. D'Esopo: I think there are two reasons: the selection of the patient, the thing that makes him a candidate for thoracoplasty in the first place; and, second, the fact that the cavity sloughing surface is reduced so it is rather small.

Dr. Julius Wilson: One would certainly conclude from the statistics that it is a good thing to have these necrotic lesions preserved in the body and spilling out occasionally a few bugs at the time a patient has a cold, because that's the story of our thoracoplasty if we watch the sputum carefully.

Dr. Norman Wilson: It has been implied that your thoracoplasty is successful because you are dealing with a better immunologically balanced patient. I don't think that's true at all. The criteria which Nick has set down have never guided me in accepting patients for thoracoplasty. I've done a high percentage of all my thoracoplasties, even pre-drug era, as primary procedures, and have done them at the time when pneumothoraces were the alternate procedures which might have been considered in each individual case. Now I'd like to ask a question. In the pre-drug era when medical treatment put patients to bed, they had cavities and on bed rest they closed their cavities. They stayed in bed until you told them to get up and stayed in the institution as long as you told them. They reached an end point, a target point of medical treatment at which you interpreted that their resistance had then reached a place where they could be discharged to life again, and yet there were 25 to 30 per cent exacerbations in that group of patients as compared to an average of 3 to 5 per cent in thoracoplasty patients. I think, if you don't agree to that, you must agree that you discharged patients to go back to living in the old days when you thought they were not in immunological balance. Is that true or not?

Dr. Tucker: I think Norm is directing that to Nick, but, as middle man here, I would say that the question really is whether the patients submitted to thoracoplasty are a more select group than the total group treated. It is my impression that they are distinctly, in spite of the fact that your indications for thoracoplasty appear to have been wider. If I may, I'm going to intercept that question, Norm, in that way, come back at you and ask you what, in your opinion, are the indications for resection as long as thoracoplasty is so wonderful?

DR. NORMAN WILSON: That's an easy one for me to answer. I think that we should resect the things which experience has taught us we fail with with other treatment.

DR. TUCKER: So you would reserve resection, either small or large, as a secondary procedure most of the time?

DR. NORMAN WILSON: That depends on many factors. For instance, if I had a cavity in the anterior segment of the upper lobe, I would resect it because I would have to destroy too much lung function to collapse it. I don't like collapsing the anterior portion of the chest because then you interfere with the function of the sternum, and elevation on respiration is too great. If the same cavity were in the apical posterior segment in a suitable position, perhaps I'd collapse it.

DR. TUCKER: Anyone want to take exception? Nick?

DR. D'ESOPO: Well, I don't think we know anything about the indications for resection. I think we are learning all the time. I think one can have certain habits about resection, but I don't think we know the indications.

DR. TUCKER: Julie, what do you think are the indications?

DR. JULIUS WILSON: It seems quite anomalous that we came to know the indications for pneumothorax and gave it up and have just come to know the indications for pneumoperitoneum. When resection is most popular, we don't know the indications at all for that.

DR. TUCKER: Gordon, what do you think are the indications for resection?

DR. MEADE: Well I think that there were several papers here at this meeting which discussed this much more thoroughly than we can on this program; but, in our experience, I think the indications for resection are those cases which have not responded, or cannot be expected to respond, to chemotherapy or, in some instances, thoracoplasty, leaving out the pneumothorax because we have in our own cases practically given up its use.

DR. TUCKER: I think that Nick D'Esopo has come to be associated with localized resection in a way that has perhaps been unfair to Nick. He has been advocating an investigation along that line. He has not been advocating it as a common practice. At any rate he's had to bear that cross and I'm going to come back at him and say, with good chemotherapy, which has led to reaching the target point as you now have defined that, Nick, do you think there is any place in such a patient for collapse?

DR. D'ESOPO: In patients who have reached the target point, I would say no. The cavities are closed and the cultures are negative.

DR. TUCKER: And what is your present position about resection in that individual?

DR. D'ESOPO: Well, we know that at that point when cultures are negative and cavities closed the organisms often cannot be cultured even though they may still be present. We don't know yet whether resection is indicated or not.

DR. NORMAN WILSON: I don't think any of us advocate the collapse of an inspissated cavity or an inspissated focus.

DR. D'ESOPO: No; I said I didn't think it was indicated. I thought you implied that it actually might be detrimental.

DR. NORMAN WILSON: No. I meant if you decided to treat one, you would treat the inspissated focus with resection.

DR. TUCKER: I want to ask Giles Filley, is the relative impairment of function with a localized segmental resection, or a wedge resection of the upper lobe for unilateral upper lobe tuberculosis, greater than following a thoracoplasty type of procedure for that same type of lesion?

DR. FILLEY: I think, in the absence of any complications, particularly pleural, that resections of that magnitude will be associated with less loss of function than will thoraco-

plasty. But that's only because the thoracoplasty almost inevitably encroaches on some normal tissue, whereas the resection can usually be quite sharply limited to the diseased area.

DR. TUCKER: Would you say, however, that the incidence of localized infection is sufficiently great to modify that answer?

DR. FILLEY: I'm afraid so, yes.

DR. TUCKER: How common does anyone think it is? Norm?

DR. NORMAN WILSON: Well, if you talk about wedges, I would say it is extremely low. Personally I don't call a wedge a resection.

DR. TUCKER: What about a subsegmental resection?

DR. NORMAN WILSON: When you take a piece of the lung out, I think you have to differentiate that from where you go down and work in the bronchial system.

DR. TUCKER: There is some complication with just a thoracotomy of course.

DR. NORMAN WILSON: But if you take localized resection of all kinds, I think statistics show, as they appear in the literature now, that you have to at least bat around 5 per cent complication rate; maybe it's a little bit greater than that.

DR. TUCKER: Norm, here's another question. Do you think that the immediate availability of a skilled thoracic surgery team influences the use of collapse procedures in an institution?

DR. NORMAN WILSON: It should. I think it takes a much better surgeon to do a safe resection than to do any chest-wall procedure. I suppose that is what your question is implying.

DR. TUCKER: Oh, it's implying a lot of things.

DR. NORMAN WILSON: Besides that, another point is that it requires much more in the way of meticulous postoperative care. I think that is one of the most important things in differentiating those two.

DR. TUCKER: We'll ask Julie Wilson the same question.

DR. JULIUS WILSON: Let me hear the question again. Well there is no question at all that the availability of a skilled thoracic surgeon influences the use of pneumothorax, pneumoperitoneum, or anything else. The only thing I want to insist on is that we don't set our mind on one form of treatment that we are going to try on two patients out of three or three patients out of four. That's the usual way it happens.

DR. NORMAN WILSON: Julie, you mean that because a man can do a resection he shouldn't resect everything he sees.

DR. JULIUS WILSON: Right.

DR. TUCKER: I'm getting to some loaded questions, as perhaps you've detected, and I'm coming back at you, Norm. Have you any idea why the certain loss of function with certain surgical procedures is regarded by the surgeons with equanimity while the possible loss of some function in pneumothorax scares off a good many internists?

DR. NORMAN WILSON: I think we can answer that question very directly. We have measured the loss of function with these procedures done in various ways. You know that. In Boston we turn to Dr. Gaensler and his group; in Saranac Lake they turn to Dr. Wright; Dr. Motley and his group, here. All of these groups have helped us answer that question. The fundamental issue is that with pneumothorax I think you have a more unpredictable loss. You don't know where your loss is going to land. I can tell you pretty well when I do a five-rib thoracoplasty in a certain fashion what the loss in that patient is going to be; not because I know anything about it, but because Dr. Wright and Dr. Gaensler have told me what it is. Dr. Wright told me, Dr. Filley, that the plombage thoracoplasty, if you will forgive me for talking about that, Bill, illustrates the point. When

you stay above the sixth rib and don't create unnecessary collapse, there is an almost immeasurable small loss of function. Is that true?

DR. FILLEY: That's true.

DR. TUCKER: Would you say that that causes the least of any measures we have discussed today, Giles?

DR. FILLEY: As low as any, not including the very small resections. You can't measure any change in most wedge resections.

DR. TUCKER: What about the small subsegmental resections?

DR. FILLEY: I think the answer to that is in the simple statistical difference between complications in plombage thoracoplasty and complications in subsegmental resection.

DR. NORMAN WILSON: This is too important to let ride because I think this means people's lives. That's the reason I think it's important. Now, Dr. Filley, will you not agree that, if I open a patient's chest and don't take any nubbin out, he will lose somewhere from 20 to 30 per cent of his function due to pain, an immobile chest wall; and if that patient already has emphysema and is on the margin of pulmonary insufficiency that he is much more apt to be thrown into it than with other procedures?

DR. FILLEY: Certainly, on a temporary basis though.

DR. NORMAN WILSON: Well he has to live through that, you know, before he can get to the later phase.

DR. TUCKER: We had some excellent evidence on that subject from St. Albans this morning. It is perfectly apparent to this audience that the kind of answers on a subject such as this will depend on the persons participating. It is equally apparent that no one from the west coast is on the panel. This was deliberate for two reasons. One, I wanted to call on my friends to sit up here with me because I felt more free to abuse them, and they have responded very kindly. The other reason was, of course, certain knowledge that in the audience many people from California would be present; thus I planned a little time to give them to ask questions or possibly answer questions. We will now have perhaps ten minutes of discussion from the floor and anyone wishing to discuss please go to one of the microphones in the aisles. Dr. Cabot Brown, do you have a question you would like to ask or answer?

DR. BROWN: I'm almost afraid to start. Several things I was very interested to learn. One is that we now regard chemotherapy as the basic therapy, and we wonder whether the addition of pneumoperitoneum to that is effective or not if the cavity is three, four, or five centimeters across; whether pneumoperitoneum contributes anything to that. Out here at least, we had been using pneumoperitoneum for something like fourteen or fifteen years before we had access to streptomycin at less than $40 a gram. We used to close lots of cavities; whether in spite of pneumoperitoneum or because of it, I don't know. But at least we used it. We certainly closed a great many more with pneumothorax; we still do. Perhaps we are a little fuzzy in our thinking; I don't know. But if you could hospitalize, back in 1928, a patient with a minimal lesion or even a moderately advanced (cavitary) lesion for perhaps four months and then have her home for perhaps three or four more months and back at work in eight months without chemotherapy, I don't see that chemotherapy has added much to the treatment of such a patient. In fact, we still do it that way. Maybe we're wrong, but our results are pretty good.

DR. TUCKER: Your time is up, Cab. Harold Trimble, we're all waiting to hear from you. I'm also going to give you just three minutes, Harold.

DR. TRIMBLE: Thanks a lot. I think there is wonderful agreement here. The only disagreement is between surgeons who are not medically trained and medical men who are not surgically trained. And the medical man handles the patient through to the end and

after all has a much longer period of time. I know something about Dr. Overholt's figures. I talked to him about a lot of these things. I couldn't find out why he didn't have a long time follow-up. A lot of patients come from places where they can't get to a follow-up spot, just like our problem is. We have made a very recent study on this. We're just in the process of getting our figures through and I have a few preliminary ones which I won't bore you with, except to say that there are figures available or will be shortly. These figures are not very much different from those we published five years ago, but there are a lot more of them. The graph shows just about the same in percentages. This business of chemotherapy is very interesting to us in the thing that we're specialists on. We don't have the figures as yet because our present use of chemotherapy, as with most other men, only goes back about six or seven years. We are using it now combined with other therapy. On this basis we are speculating on the fact what it will not do; as has been brought out, probably with pneumothorax, which we still use as a secondary procedure, it will cut down complications and, second, in pneumoperitoneum and pneumothorax maybe let us keep up this collapse for a shorter period of time. After all, I think the answer to this is a long-time follow-up with patients on what actually happens after we get a good collapse. I think that will probably give us the answer. And there is just one thing that wasn't mentioned here at all today, which is the bronchus. I think it makes a difference because you can't say you are going to resect this person because maybe his bronchial openings have active tuberculosis and you are blocked. What are you going to do for the patient then? The bronchus is very important to us and it seems to me it is largely disregarded.

DR. TUCKER: Thank you, Harold. Any other comments or questions? Either this is a very live subject on which we all agree or a very dead one. Well, as long as you are not taking advantage of the opportunity, I have what I consider a very key question on this. I am going to direct it to several of the members of the panel in turn. With the availability of good effective chemotherapy today and considering all the advantages and disadvantages of collapse procedure, what in your opinion is the main indication today for pneumothorax? We'll start with Nick D'Esopo.

DR. D'ESOPO: You said you wanted opinions. Well, the indications for pneumothorax would be the patient with cavity which did not close with chemotherapy and probably would not close on pneumoperitoneum. I might even try pneumoperitoneum for him if his cavity could not be resected and could not be collapsed with thoracoplasty. In other words, I'd feel fairly desperate before I used pneumothorax.

DR. TUCKER: In other words, Nick, you would start with chemotherapy; possibly use pneumoperitoneum; and, if there was a contraindication to thoracoplasty or resection, you might try pneumothorax. Well, that's getting it down pretty fine. Now Gordon Meade, what is your answer to that same question?

DR. MEADE: I would agree pretty much with Nick. I would like to add, too, the patient who has become completely resistant to most of the antibiotics that we have available. That would also enter into consideration.

DR. TUCKER: Julie?

DR. JULIUS WILSON: There is one indication that hasn't been mentioned. That's hemoptysis. That's the best possible way we have to control hemoptysis. But that's beside the main objective of the question. I certainly wouldn't resect the lung for hemoptysis or do a thoracoplasty. In a young person who had a moderately advanced lesion, unilateral, I would consider pneumothorax as a treatment along with chemotherapy. One cannot tell whether the cavity will or will not be closed by chemotherapy. The mere fact that a certain percentage might get converted sputum or close cavities on chemotherapy

doesn't do the others any good. Waiting for the organisms to develop resistance on the basis of an open cavity is the poorest thing to do with regard to pneumothorax.

DR. TUCKER: Norman?

DR. NORMAN WILSON: I hesitate to answer this since Dr. Trimble intimated I had no medical training, although I see my old mentor, Dr. Amberson, sitting in the back of the room. Maybe he will back me up in spite of Dr. Trimble. But I might add that, if I wanted to give pneumothorax in my district, my medical men wouldn't permit me to do so.

DR. TUCKER: Now I'm coming to the other question. With the availability again of good effective chemotherapy today and considering the advantages and disadvantages of the other procedure we have been primarily talking about, what in your opinion, Gordon, is the main indication for pneumoperitoneum today?

DR. MEADE: I think the main indication that we would consider would be the patient who has predominately bilateral cavitary disease. It would be used as an adjunctive procedure until we were able to reach a point with chemotherapy where surgery could be used on one side or another; in other words a situation where you are not able to use such a procedure as thoracoplasty or resection.

DR. TUCKER: Julie?

DR. JULIUS WILSON: I think I'd agree with that entirely—progressive tuberculosis, bilateral cavitation as an adjunct to bed rest and chemotherapy.

DR. TUCKER: Nick?

DR. D'ESOPO: Yes, I think so. Bill, may I say a final word. I'd like to sum up my own point of view. I think this: that today we don't know how to treat tuberculosis really. We have various forms of therapy: rest therapy, chemotherapy, collapse therapy, surgical collapse, resection, and no doubt all these form a pattern. We don't know that pattern, and every time we introduce a new thing the relationships of all the other things change. The thing we have introduced most recently, I think, is prolonged chemotherapy. Therefore, our relationships between prolonged chemotherapy, temporary collapse, permanent collapse, have changed and we really don't know what the best pattern is for the patient. I think we must distinguish what we should do and what is best for the individual patient we have at hand and what we are trying to learn in the way of organized study.

DR. TUCKER: Nick, I think that is as good a summing up of the present status as it is possible for anyone to give and it precludes the necessity for your moderator to attempt to summarize. And now one final question, submitted by Julius Wilson of Philadelphia which I shall direct to Dr. D'Esopo. What did Lady Macbeth refer to (in Act V, Scene, 1) when she said: "Yet here's a spot!" "Out, damned spot!" "What's done cannot be undone. To bed, to bed, to bed." Did Shakespeare or Bacon, if you will, foresee the modern attack on the deadly "necrotic focus," the fearful "tuberculoma," and the ominous "coin shadow"? If so, we should note the final emphasis on prolonged bed rest.

(*Unlike the question, Dr. D'Esopo's answer was unfortunately not recorded for posterity. Ed.*)

NOTES

ANNUAL MEETING OF THE AMERICAN TRUDEAU SOCIETY—1954

The American Trudeau Society, medical section of the National Tuberculosis Association, invites the submission of scientific papers for presentation at its next annual meeting in Atlantic City, New Jersey, May 17 to 21, 1954.

Abstracts

Abstracts of papers to be offered for presentation should be submitted in *duplicate* not later than December 1, 1953, with an absolute deadline of January 1, 1954, to Dr. Julius L. Wilson, Chairman of the Medical Sessions Committee, Henry Phipps Institute, 7th & Lombard, Philadelphia 47, Pa.

Abstracts should be limited to a 300-word summary including important data and conclusions. Charts and tables should be attached to aid in the selection of papers.

The names, titles, and complete addresses of the senior author and co-authors should be included in each abstract. The author who is to present the paper must be the first author listed in the abstract.

All abstracts and papers will be reviewed by the Medical Sessions Committee and, when necessary, by experts in special fields in order to select those containing the most interesting material. Final selection will be on a competitive basis.

Subjects for presentation may include all scientific aspects of tuberculosis and nontuberculous respiratory and cardiopulmonary disease as well as the results of investigative work bearing on these subjects.

Those wishing to present subjects of a confidential nature from the armed forces or other sources must clear the material through official channels *before* submitting the abstracts to the Chairman of the Medical Sessions Committee.

Papers

Subsequent to review of the abstracts by the Medical Sessions Committee, papers will be chosen on a competitive basis from among the abstracts for presentation at the annual meeting. Authors will be notified by February 1, 1954, if their papers are to be read.

A double-spaced typewritten manuscript must be prepared in *duplicate* to be presented to the moderator of the session at the time the speaker presents his paper at the annual meeting.

Papers presented at the annual meeting must be original contributions which have not previously been presented or published. All such papers should be considered as belonging exclusively to the National Tuberculosis Association and should not be submitted for publication elsewhere without the advance permission of the National Tuberculosis Association.

Abstracts of all papers given at the annual meeting will be published in the annual *Transactions* of the National Tuberculosis Association. All papers will be submitted to THE AMERICAN REVIEW OF TUBERCULOSIS, but publication in the REVIEW will be subject to the decision of the Editor.

The time allotted for presentation of papers at the annual meeting will be strictly limited by the committee in order to permit adequate discussion.

Participants in the program are reminded of the fact that travel expenses to the annual meeting are not paid by the National Tuberculosis Association.

RENEWAL OF SUBSCRIPTIONS TO THE AMERICAN REVIEW OF TUBERCULOSIS

The Bylaws of the American Trudeau Society require the suspension of subscriptions to THE AMERICAN REVIEW OF TUBERCULOSIS when current dues remain unpaid as of March 31.

In years past, every effort has been made to provide a sufficient number of copies of April and subsequent issues to provide complete files for delinquent members, but mounting publishing and handling costs will make it necessary, in 1954, for the publishers to limit print orders, each month, to the actual number of paid subscriptions on hand when we go to press.

To help us to protect members against any resulting breaks in their REVIEW files, the earliest possible attention to the annual statements mailed in December, 1953, is particularly invited.

ANNUAL MEETING OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS

The 20th Annual Meeting of the American College of Chest Physicians will be held in San Francisco, California, June 17–20, 1954. Physicians interested in presenting scientific papers on any phase in the diagnosis and treatment of heart and lung disease should send a 100-word abstract, not later than January 1, 1954, to Dr. Edgar Mayer, Chairman of the Committee on Scientific Program, 850 Fifth Avenue, New York 21, New York.

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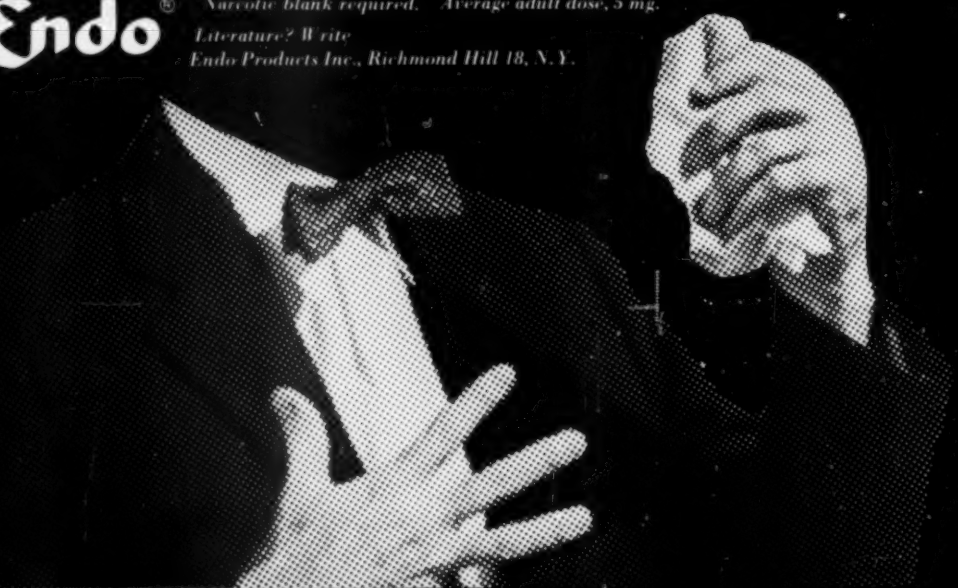

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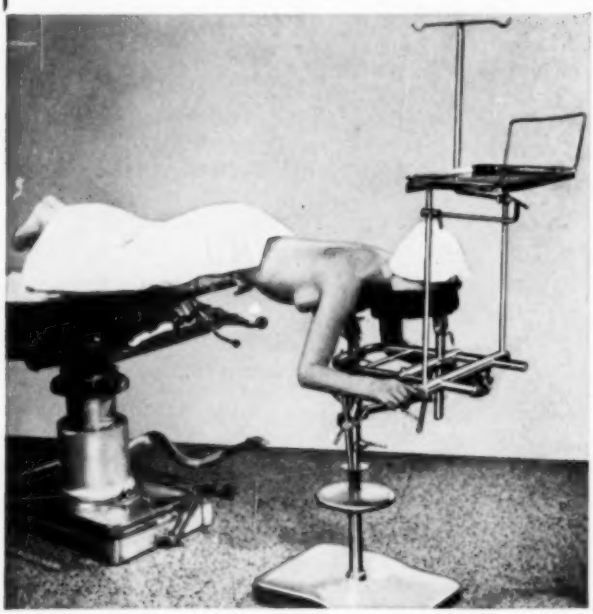

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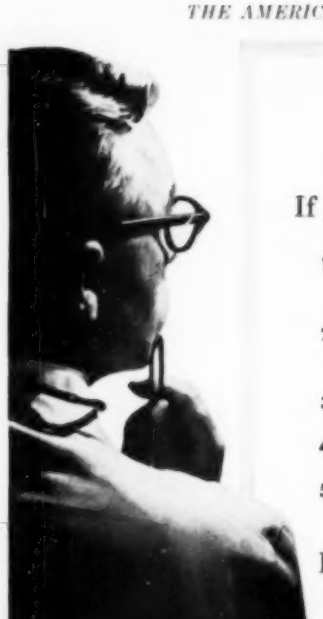

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Staff physician, 200-bed tuberculosis sanatorium located in Michigan. American or Canadian graduates only eligible for Michigan license. One-year approved internship. Tuberculosis experience desirable but not essential. Salary $8,000 and up depending on qualifications and experience. Box 131, American Review of Tuberculosis, 280 Madison Avenue, New York 16, N. Y.

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STAFF PHYSICIANS: 700-bed, modern state tuberculosis hospital, located in town 25,000. Experience not essential. Eligibility North Carolina license desired. Salary depends on qualifications. Apply Medical Director, Eastern North Carolina Sanatorium Wilson, N.C.

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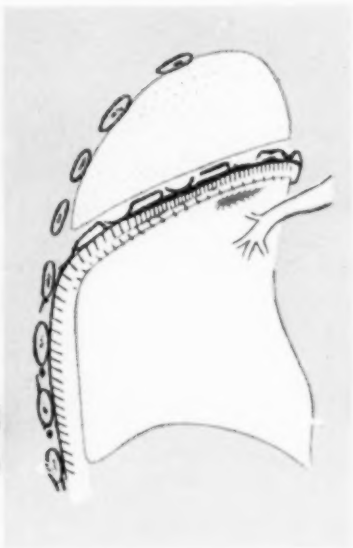

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50th ANNIVERSARY ★ NATIONAL TUBERCULOSIS ASSOCIATION

Annual Meeting, Atlantic City, New Jersey, May 17-21, 1954

The 50th Anniversary of the National Tuberculosis Association will be celebrated at its Annual Meeting to be held in Atlantic City, New Jersey, May 17-21, 1954.

Three adjacent hotels, the Ambassador, Chelsea and Ritz-Carlton, will serve as headquarters. Sessions and conferences will be divided among the three hotels with no one hotel marked exclusively for medical or community service programs.

Applications for rooms should be made directly to the hotel of choice. In the event that the hotel is unable to provide the desired space, requests will be turned over to the Convention Bureau, which will clear requests with another one of the cooperating hotels.

Hotels offering accommodations through the Atlantic City Convention Bureau and their rates are:

AMBASSADOR, Boardwalk at Brighton Avenue
Singles —$6.00-$18.00 Parlor Suites —$20.00-$45.00
Doubles—$8.00-$20.00

CHELSEA, Boardwalk at Park Place
Singles —$6.00-$12.00 Two Rooms—Connecting Bath—
Doubles—$8.00-$16.00 $12.00-$18.00
Parlor Suites —$24.00-$30.00

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Singles —$5.00-$ 7.00 Two Rooms—Connecting Bath—
Doubles—$7.00-$10.00 $10.00-$16.00

FOX MANOR, 2720 Pacific Avenue
Singles —$5.00-$ 8.00 Two Rooms—Connecting Bath—
Doubles—$6.00-$12.00 $15.00-$25.00
Three Rooms—Connecting Bath —$18.00-$30.00
Parlor Suites —$15.00-$30.00

MARK, 100 South Chelsea Avenue
Singles —$5.00-$ 7.00 Two Rooms—Connecting Bath—
Doubles—$6.00-$ 8.00 $14.00-$16.00
Motel Rooms —$10.00-$16.00

RITZ-CARLTON, Boardwalk at Iowa Avenue
Singles —$6.00-$ 8.00 Two Rooms—Connecting Bath—
Doubles—$8.00-$16.00 $20.00
Parlor Suites —$35.00

IMPORTANT ANNOUNCEMENT

THE AMERICAN REVIEW OF TUBERCULOSIS has made available to its readers a section devoted to classified advertising pertaining to positions available and wanted. Since there have been so many requests for this type of service in the tuberculosis field, the Editorial Board of THE AMERICAN REVIEW OF TUBERCULOSIS decided to include a classified section at a nominal charge for each entry.

- **Cost per advertisement of 25 words or less will be $3.50, additional words 15 cents each.**
- **Bold Face Semi-display will be $5.00 per insertion for 25 words or less, additional words 20 cents each.**
- **Post Office Box numbers will be an additional 75 cents per advertisement.**
- **Address all classified advertisements, with check or money order enclosed, to:**

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